

UNITED STATES DISTRICT COURT  
FOR THE  
DISTRICT OF MASSACHUSETTS

---

JOHN HANCOCK LIFE INSURANCE  
COMPANY, JOHN HANCOCK  
VARIABLE LIFE INSURANCE  
COMPANY, and MANULIFE INSURANCE  
COMPANY (f/k/a INVESTORS  
PARTNER LIFE INSURANCE  
COMPANY),

Plaintiffs,

v.

ABBOTT LABORATORIES,

Defendant.

---

CIVIL ACTION NO. 05-11150-DPW

**AFFIDAVIT OF STEPHEN J. BLEWITT**

**CONTINUATION OF EXHIBITS**

**PLs' IA**

**CONFIDENTIAL**

**ABT – 773**

**Descriptive Memorandum**

*November 2000*

**Abbott Laboratories**

Nov. 1, 2000

Hancock – ABT-773

**CONFIDENTIAL**

ABBT 0006648

**ABT-773***Opportunity Overview*

ABT-773 pertains to a promising new class of antibiotics known as ketolides. ABT-773 is likely to have activity against resistant strains of bacteria and will, therefore, compete effectively against currently marketed antibiotics. The compound is currently in Phase IIb trials. It is scheduled to begin in phase III clinical trials in Q4, 2000 and has an expected U.S. launch date in Q1, 2004. Ex-U.S. launches are projected in 2004 for Europe and Japan.

Product features such as high efficacy, activity against resistant strains of bacteria and convenience should enable it to compete against both Zithromax and newer agents such as the quinolones. Dosing is expected to be once-a-day. A 5-day convenience pak at a competitive price will help maximize sales.

*The US Market*

The overall antibiotic market in the U.S. reached \$8.9 billion in sales in 1999. The tab/cap segment is the largest; sales in 1999 were \$5.7 billion. The I.V. and oral suspension segments are comparatively smaller; total sales topped \$2.1 and \$1.1 billion, respectively.

Tab/cap and oral suspension prescription volume had been declining 1-2% per year in the period of 1995-1998, due to more appropriate prescribing in the face of increasing resistance. However, total tab/cap prescription volume recovered in 1999 and grew 6.3%. Even in the face of negative pressure on antibiotic use, dollar sales in the U.S. have continued to increase, particularly in the tab/cap market. This is due to the trend of replacing relatively low-cost generic agents with higher priced premium antibiotics. The market is willing to bear higher costs for agents that satisfy unmet needs. The I.V. market has grown slightly in terms of sales, also being driven largely by the replacement of generic agents with more costly branded agents.

Macrolides, largely fueled by the gains of Zithromax, have seen significant growth in terms of both prescriptions and sales. Zithromax prescriptions far outnumber those of other competitors, while its sales have nearly surpassed those of the sales leader, Cipro. Historically, quinolones saw relatively limited use for community respiratory tract infections (RTIs) because of poor Gram-positive coverage and sub-optimal adverse event profiles. Newer quinolones such as Levaquin have been successful in achieving more widespread use by virtue of its improved activity and adverse event profile. Levaquin currently accounts for approximately 30% of quinolone market share. It is anticipated that recent quinolone introductions (Avelox, Tequin) will build upon the RTI momentum established by Levaquin. The growth of the macrolide and quinolone classes has come largely at the expense of cephalosporins and generic agents such as erythromycin and penicillin.

The following table shows 1999 tab/cap sales and prescriptions by class/product

	Sales			TRXs		
	Sales (\$MM)	Share	CAGR <sub>95-99</sub>	TRXs (MM)	Share	CAGR <sub>95-99</sub>
Penicillins	\$148.3	2.6%	-1.0%	52.5	23.7%	-5.6%
Cephalosporins	\$980.9	17.2%	-5.8%	37.9	17.1%	-3.5%
Ceflin	\$383.9	6.7%	1.8%	5.0	2.3%	-1.0%
Cefzil	\$188.7	3.3%	12.5%	2.7	1.2%	11.3%
Other	\$408.3	7.1%	-14.7%	30.1	13.6%	-4.8%
Ext. Spec. Macrolides	\$1,595.6	27.9%	19.9%	36.1	16.3%	20.8%
Biaxin	\$690.5	12.1%	6.1%	11.3	5.1%	1.2%
Zithromax	\$891.1	15.6%	42.1%	24.4	11.0%	41.5%
Other	\$14.0	0.2%	21.0%	0.4	0.2%	53.0%
Quinolones	\$1,622.1	28.4%	17.0%	24.0	10.8%	11.7%
Cipro	\$902.5	15.8%	8.3%	14.1	6.4%	5.1%
Levaquin	\$529.4	9.3%	NA	7.0	3.1%	NA
Other	\$190.2	3.3%	-2.2%	3.0	1.3%	-6.4%
Augmentin	\$778.1	13.6%	17.8%	10.7	4.8%	11.8%
Other Classes	\$590.5	10.3%	-1.1%	60.4	27.3%	-4.1%
TOTAL TAB/CAP	\$5,715.4	100.0%	8.9%	221.5	100.0%	0.1%



*U.S. Market Projections*

Resistance to antibiotics is likely to increase, creating opportunities for new agents with activity against resistance. Physicians will be urged to choose agents with an appropriate spectrum of activity relative to the infection being treated. Resistance will increasingly become part of the promotional mix for emerging agents. The ability of an agent to treat resistant strains and the real or perceived ability to slow or prevent resistance development (mutation prevention concentration, low mutation frequency, structure-activity relationships, etc) may confer competitive advantage to such agents.

- Quinolones, which historically have seen limited use in community-acquired respiratory infections, will become a significant class in this segment as new agents from this class are launched that specifically target RTIs.
- The market will become more competitive as new agents enter both the community segment (ketolides, quinolones) as well as the nosocomial segment (oxazolidinones, streptogramins, evernimomycins, peptides, others).
- Several key branded antibiotics will lose patent exclusivity over the next three to five years.. This may create an opportunity in the pediatric market as the top three pediatric brands (Augmentin, Cefzil, Zithromax) are among those losing patent exclusivity.

Antiviral influenza and cold therapeutics, as well as an increasing number of antibacterial vaccines may have a negative impact on antibiotic prescriptions.

*The Ex-U.S. Market*

Ex-U.S. sales of antibiotics totaled \$11.7 billion in 1999. Tab/cap represents the largest segment, with sales of \$9.4 billion from 770 million total prescriptions. Total Rx growth has been flat, with a 1996-99 CAGR of 0.5%. The use of antibiotics is predicted to slowly decline due to more judicious use of antibacterials in the face of increasing bacterial resistance.

Ex-U.S., the quinolone class accounted for 8% of total tab/cap market prescriptions (62 million Rxs) and 13% of sales (\$1.2 billion). Ciprofloxacin is the market leader ex-U.S. with approximately 47% of the quinolone market Rxs (29 million Rxs) and 44% (\$530MM) of sales. Levofloxacin launched in many European markets in 1998/1999 and holds approximately 14% Rx share of the European quinolone market and 0.8% of the overall tab/cap market. Although grepafloxacin and trovafloxacin also launched in some European countries in 1999, both products were recently pulled from the market due to liver toxicity and other complications. Moxifloxacin launched in Germany in Q4 1999, but has not yet been approved in other markets. In Japan, levofloxacin launched in 1994 and still commands a 65% Rx share of the quinolone market and 10% of the Japanese tab/cap market overall. Japan accounts for approximately 80% of ex-U.S. levofloxacin sales (\$370MM).

*Scientific Rationale for ABT-773*

The likely profile of ABT-773 justifies further development:

- ABT-773 pertains to a new class of antibiotics.
- Good activity against resistant gram + organisms, particularly macrolide resistant *S. pneumoniae*.
- Convenience, safety, and tolerability profile competitive with Z-pak.
- Oral Suspension and I.V. forms enabling penetration into pediatrics and hospital segments.

*Clinical Studies*

The safety and efficacy of ABT-773 in AECB were studied in a multi-center Phase II clinical trial conducted between January and April of 1999. Dosing regimens of 100mg TID and 200mg TID were tested. Of the 169 enrolled patients, 159 were clinically evaluable and 96 were both clinically and bacteriologically evaluable. The following chart summarizes the results.

Presumed Bacterial Eradication	ABT-773 100mg TID	ABT-773 200mg TID	Overall Eradication
<i>S. pneumoniae</i>	100% (13/13)	90% (9/10)	95% (22/23)
<i>M. catarrhalis</i>	100% (6/6)	100% (7/7)	100% (13/13)
<i>H. influenzae</i>	96% (23/24)	92% (24/26)	92% (47/50)
<i>H. parainfluenzae</i>	100% (6/6)	88% (7/8)	93% (13/14)

Clinical Response	ABT-773 100mg TID	ABT-773 200mg TID
Cure	96% (77/80)	92% (73/79)
Failure	4% (3/80)	6% (3/48)

Clinical and Bacteriological Response	ABT-773 100mg TID	ABT-773 200mg TID
Cure	96% (46/48)	94% (45/48)
Failure	4% (2/48)	6% (3/48)

Adverse Events	ABT-773 100mg TID	ABT-773 200mg TID	Overall
Taste Perversion	5% (4/84)	8% (7/85)	6.5% (11/169)
Diarhea	11% (9/84)	6% (5/85)	8% (14/169)
Nausea	2% (2/84)	2% (2/85)	2% (4/169)
Abdominal Pain	1% (1/84)	2% (2/85)	2% (3/169)
Headache	2% (2/84)	1% (1/85)	2% (3/169)
Rash	2% (2/84)	1% (1/85)	2% (3/169)
Dyspnea	2% (2/84)		1% (2/169)
Elev. Liver Funct. Test	1% (1/84)	1% (1/85)	1% (2/169)
Fever		2% (2/85)	1% (2/169)

*Patent Status*

ABT-773 will have patent exclusivity through 2016.

- Appendix 1

## Key Emerging Competitors

Generic	Brand	Company	Class	Status
moxifloxacin	Avelox	Bayer	Quinolone	Approved by FDA 12/13/00
gatifloxacin	Tequin	BMS	Quinolone	Approved by FDA 12/21/00
gemifloxacin	Factive	SKB	Quinolone	Filed NDA 12/15
T-3811	TBD	BMS/Toyama	Quinolone	Phase I
telithromycin	Ketek	Aventis	Ketolide	Filed NDA 3/00
linezolid	Zyvox	Pharmacia	Oxazolidinone	Approved by FDA Q2 '00

**PLs' IB**

## NOVEMBER 2000 - "TOP" ISSUES

## Key Issues/Decisions/Events

Area  
ABT-378 Kaletra  
Regulatory

## Issue/Decision/Event

## Progress

Redacted

ABT-492  
Clinical

ABT-518  
Toxicology/  
Metabolism

Key tox finding was hepatotoxicity in one-month rat study. In-vitro and in-vivo data indicate a potential for mechanism based drug interactions.

The Phase I first-in-man protocol has been designed to address these issues. Additional tox and metabolism studies planned to address this issue.

ABT-594

USAN approval for the generic / chemical name for ABT-594 was received. The United States Adopted Name for ABT-594 (A-166594.47) is edanilcline tosylate (e-ba-ni-klan to-se-lat.)

ABT-627  
Formulation  
Manufacturing

R.P. Scherer (Tampa) is a single site for production of drug product. Site audit revealed deficiencies which will delay production of Phase III clinical supplies but will NOT delay initiation of Phase III trials.

Alternate R.P. Scherer sites as well as alternate vendor options are being explored. Deficiencies are being corrected and will be resolved prior to production of Phase III clinical supplies in 1/01.

PARD

French authorities have raised issue of acid treated gelatin in our SGCs (also used in Kaletra and Norvir).

PARD will investigate alkaline treated SGCs for possible switch in the NDA runs.

ABT-773  
Regulatory

An end of Phase II meeting with FDA was targeted for the end of September/mid October timeframe, but rescheduled to the end of November at the request of FDA.

Meeting with FDA was held on November 27<sup>th</sup>. QT effects are the current hot topic for the FDA, and was reflected in the changes they requested to the Phase III program. They also requested an acute tox study in dog to further evaluate cardiac effects. The required "body of evidence" for obtaining a resistance claim for *s. pneumoniae* was discussed and the FDA recommendation included having an IV formulation to get bacteremic patients and more serious CAP infections.

Regulatory uncertainties over how to deal with the ketolide/macrolide class regarding QT interval effects.

FDA concern is whether ketolides behave like macrolides and whether there may be a class effect. They also discussed whether a Phase I study should be conducted in subjects with

HIGHLY CONFIDENTIAL

ABBT0017833

**PLs' ID**



Jeanne M  
Fox/LAKE/PPRD/ABBOTT  
11/20/2000 04:11 PM

To John M Leonard/LAKE/PPRD/ABBOTT@ABBOTT, Jerald J  
Wenker/LAKE/PPD/ABBOTT@ABBOTT, Lawrence E  
Roebel/LAKE/PPRD/ABBOTT@ABBOTT  
Arthur J Higgins/LAKE/PPD/ABBOTT@ABBOTT, Carl  
Craft/LAKE/PPRD/ABBOTT@ABBOTT, George  
Aynlian/LAKE/PPRD/ABBOTT@ABBOTT, Reid  
Patterson/LAKE/PPRD/ABBOTT@ABBOTT, Julia Y  
Hui/LAKE/PPRD/ABBOTT@ABBOTT, William M  
Bracken/LAKE/PPRD/ABBOTT@ABBOTT, Maria M  
Paris/LAKE/PPRD/ABBOTT@ABBOTT, Joaquin M  
Valdes/LAKE/PPRD/ABBOTT@ABBOTT, David D  
cc Morris/LAKE/PPRD/ABBOTT@ABBOTT, Jie X  
Zhang/LAKE/PPRD/ABBOTT@ABBOTT, Carol S  
Meyer/LAKE/PPRD/ABBOTT@ABBOTT, Robert K  
Flamm/LAKE/PPRD/ABBOTT@ABBOTT, Linda E  
Gustavson/LAKE/PPRD/ABBOTT@ABBOTT, Gregory  
Bosco/LAKE/PPRD/ABBOTT@ABBOTT, Rod M  
Mittag/LAKE/PPD/ABBOTT@ABBOTT, Linda J  
Swanson/LAKE/PPRD/ABBOTT@ABBOTT, Cheryl D  
Spencer/LAKE/PPRD/ABBOTT@ABBOTT

bcc

Subject FDA Telephone Contact Report ABT-773

Attached is a contact report for a teleconference that was held with FDA today concerning ABT-773. We are now officially on clinical hold until further discussion at the End-of-Phase 2 meeting scheduled for November 27, 2000.

Call me if you have questions,

jeanne



FDA Contact Reportdoc.doc

CONFIDENTIAL  
ABBT0558681

Leonard EXHIBIT 51  
FOR I.D. 6/1/07 1.0ef

### FDA Contact Report

Compound/Product Discussed: ABT-773  
Application Type & Number: IND 57,836

Date of Contact: November 20, 2000

	Name & Title	Group
FDA Person(s) Contacted	Dr. Janice Soreth, Acting Division Director	Division of Anti-Infective Drug Products
	Dr. Mercedes Albuerne, Supervisory Medical Officer	
	Dr. Alma Davidson, Medical Officer	
	Dr. Bob Osterberg, Supervisory Pharm/Tox Reviewer	
	Dr. Terry Peters, Pharm/Tox Reviewer	
	Maureen Dillon-Parker, CSO	
Abbott Representatives	Jeanne Fox	Regulatory Affairs
	Greg Bosco	"
	Carl Craft	Venture
	George Aynilian	"
	Reid Patterson	Drug Safety
	Bill Bracken	"
	Julia Hui	"

**Subject of Call:** FDA requested this teleconference to talk about some "toxicology issues" prior to our End-of-Phase 2 meeting scheduled for next week (November 27, 2000).

**Report of Call:** The meeting began with introductions, then Maureen said she was filling in for our CSO, Jose Cintron, and asked if we had been told the subject of the call. I told her we understood the purpose to be tox, but had no specifics. Dr. Peters then began by saying that she reviewed our 3 month monkey toxicology study as well as the inspection report and has several concerns about the study. First, there is a concern because the FDA investigator found that there was active drug in some of the control samples. Second, they have knowledge which they cannot share with us regarding similar drugs that has convinced them that the monkey is not a sensitive enough species to look for the two primary toxicities they are worried about with macrolides and ketolides, hepatotoxicity and QT changes. They had advised us of their recommendation that we use the dog after the results of the one month monkey tox study, and now they are looking at a 3 month study in monkeys that they believe is flawed. Reid explained the rationale behind not using the dog since our early work in dogs indicated that emesis became so pronounced in dogs that we were unable to reach significant drug exposures, therefore we switched to monkeys. They asked whether we had done QT assessment in this study and we responded no, that our QT evaluation was done by the safety pharmacology group. They responded that they were looking for QT assessment on multiple dosing in toxicology studies, not the kind of information that came out of single dose pharmacology studies. They then stated that to meet the requirement to start phase 3, they need chronic toxicology done in two species and so they want us to do a 30-day dog study with full QT assessment done by telemetry and evaluation for hepatotoxicity. I pointed out that we have provided in our pre-meeting package specific analyses of both our hepatic safety evaluations and our QT monitoring results from the 900 plus patients that we have treated in Phase 1 and 2. Reid stated that since nothing significant was seen in any of the human data it would seem somewhat meaningless to go back and do the dog study. FDA asked to put us on hold.

When they came back after 5 minutes they said they would propose a compromise, and instead of a 30 day study, they would require a two week dog study with special emphasis on hepatotoxicity and QT, with telemetry and with a

CONFIDENTIAL  
ABBT0558682



recovery period. We agreed that it may be possible to run such a study, although we still have concerns about getting adequate exposures in the dog. I then said that our bigger concern was allowing this tox request to delay our phase 3 studies, and asked if it would be acceptable to run the tox study concurrently since the Phase 3 studies had already started. Based on FDA's reaction it was clear they were unaware that we have begun our studies. Dr. Soreth asked how we could do that prior to our end-of-phase 2 meeting. I pointed out that we had first requested a meeting in July, and it has been scheduled and rescheduled several times. I referenced the letter I sent to her in October when they cancelled the scheduled meeting the last time, which told her we would begin our trials the second week in November. I also referred to the new protocol amendments that were submitted over the last several weeks initiating the studies. She said they expected us to send the protocols to them and wait for comments before proceeding. I explained that we have received comments on at least one of the protocols and parts of the others. She wanted to know if our recent submissions stated we were planning to enroll patients now. I responded that these are our standard study start-up submissions that include information on a minimum of one investigator who can then enroll patients. I explained that we have several patients currently enrolled. Dr. Soreth was not happy with this information, and FDA put us on hold again.

When FDA came back off hold Dr. Soreth told us that they were not expecting us to begin our phase 3 studies prior to the end-of-phase 2 meeting, and that they want us to suspend enrollment at this time. In other words, we are now on clinical hold with these studies. They will discuss this information further prior to the meeting next Monday. I asked whether the 1 hour that has been allotted us next Monday will be enough. Dr. Soreth responded that it will have to be. She indicated they are probably still going to require a dog study. I commented that we do have in writing from Dr. Peters that the three-month study in monkeys should be acceptable to fulfill the requirement. We received this in response to our argument against using dog when they first raised it last year. They did not have the reviewers document in front of them, and Dr. Peters could not recall it, so they said they would go back and look through their records. She also stated that regardless, they would still have issues with the quality of the 3 month study. Reid promised to provide a written response to the issue of active drug in control samples, stated again that there was nothing significant enough to invalidate the study, and questioned whether we could get the exposures they were looking for in dogs. Dr. Peters commented that other sponsors with drugs like these manage to do dog studies. We agreed to provide an estimated timeline for a two-week dog study at Monday's meeting.

We suggested to Dr. Soreth that they also review the QT and hepatic safety assessments that were done in phase 2 since those were done at doses up to 600 mg, so there is more exposure in those phase 2 studies than we will have in phase 3. She said they will look at it.

**Action Items:** Provide a chronology showing all of the delays in getting the phase 2 meeting to happen as well as the submission of the protocols for review and the response from Dr. Peters acknowledging the 3 month monkey study as acceptable. Prepare a written response regarding the positive study drug in controls from the 3 month tox study.

**PLs' IE**

---

**FDA Contact Report**

Compound/Product Discussed: ABT-773 - End of Phase 2 Meeting

Application Type &amp; Number: IND 57,836

Date of Contact: November 27, 2000

	Name & Title	Group
FDA Person(s) Contacted	Jose Cintron, Sr. Project Mgr	Anti Infective Division
	Mercedes Albuerno, Medical Team Leader	"
	Nasim Moledina, Medical Officer	"
	Mamodikoe Makhene, Medical Officer	"
	Alma Davidson, Medical Officer	"
	Daphne Lin, Statistics Team Leader	"
	Erica Brittain, M.D., Statistics Reviewer	"
	Terry Peters, Pharm/Tox Reviewer	"
	Robert Osterberg, Pharm/Tox Team Leader	"
	Lilian Gavrilovich, Deputy Director	"
	Charles Bonnapace, Biopharm Reviewer	"
	Frank Pelsor, Biopharm Team Leader	"
	Sousan Altaie, Micro Reviewer	"
	Jean Mulinde, Medical Officer	"
	Jim Timper, Chemistry Reviewer	"
	Charles Cooper, Medical Officer	"
	Albert Sheldon, Micro Team Leader	"
	Janice Soreth, Acting Division Director	"
	John Alexander, Medical Officer	"
	Diane Murphy, Office Director	Office of Drug Evaluation - IV
Abbott Representative(s)	Greg Bosco, Sr. Product Mgr	Regulatory Affairs
	Jeanne Fox, Director	Regulatory Affairs
	Jie Zhang, Statistician	Clinical Statistics
	Joaquin Valdes, Physician	Anti Infective Venture
	Carol Meyer, Operations Manager	Anti Infective Venture
	Bob Flamm, Microbiologist	Microbiology
	Linda Gustavson, Pharmacokineticist	Clinical Pharmacokinetics
	David Morris, Statistician	Clinical Statistics
	Maria Paris, Physician	Anti Infective Venture
	George Aynilian, Associate Venture Head	Anti Infective Venture
	Carl Craft, Venture Head	Anti Infective Venture
	John Leonard, Vice President	Research & Development
	Reid Patterson, Vice President	Drug Safety

**Subject of Meeting:**

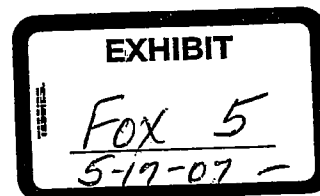
The purpose of the meeting was to introduce the oral tablet Phase 3 development plan, discuss potential issues, and address any questions regarding the plan or Phase 2 study results.

**Report of Meeting:**

The meeting began with introductions from both sides. As Carl began his presentation, Dr. Soreth stated that in case there was some misconception regarding the result of the telecon held on 11/20/00, she wanted to say that the ABT-773 program was at this point not on clinical hold.

Confidential

ABBT205257



Carl began his presentation with a slide showing the proposed indications and treatment durations we were planning to file in the NDA. He showed a series of slides which summarized all the Phase 3 studies we are planning; those starting in 2000 and those slated for 2001. This was the first time FDA saw the proposed dose-selection studies for pneumonia (CAP) and sinusitis (ABS). Dr. Brittain had a few questions regarding the objectives of the studies and the proposed interim analyses, but stated that she would be faxing us all of her comments in more detail. Carl stated that the objectives of the studies were: to pick a dose for the large, well-controlled, comparative, pivotal studies to be conducted in 2001, and to meet the specific pathogen criteria as required for the second supportive trials in the FDA guidance for CAP and ABS. There was lengthy discussion around these study designs. It was stressed to FDA that we still intend to conduct a large, well-controlled, double-blind, comparative trial for each of these indications. FDA advised us there might be a problem using Augmentin 875 mg BID for the sinusitis trial. They would prefer us to use 500 mg TID. Carl committed that we would provide the results from these two trials to FDA for review.

The next slide shown detailed our intention to request a claim for macrolide and penicillin resistant bacteria and atypical bacteria, and the supporting data we proposed to provide to support these claims. Dr. Albuerne stated that we could pool isolates for CAP and ABECB but not for ABS (we proposed pooling from all three). Dr. Soreth stated that there is currently no guidance document available addressing specific requirements for resistant claims but mentioned that there is data from other products (e.g. levofloxacin) that is available in the public domain. As far as our proposal for number of isolates, numbers >10 would be acceptable with good data for susceptible pathogens, but there has been an instance (with linezolid) where <10 was not approvable, but in that case only one or two patients had bacteremia and responded well to therapy. It was stated that a number of bacteremic patients would be required in order to adequately evaluate clinical success against penicillin resistant *Strep pneumoniae*. The comment was made that with oral therapy alone we would probably be hard pressed to find enough patients with bacteremia, that oral/IV therapy gave us a better chance. Dr. Soreth stated that FDA has not seen data supporting "macrolide resistant *Strep pneumoniae*" as a clinical concern. They also said that there is no good body of evidence supporting macrolide resistant *Strep pyogenes* either.

The next topic discussed was the ECG monitoring plan regarding the six Phase 3 studies starting in 2000. We proposed that ECG's would be performed in 5/6 of the studies. In total, we would be gathering ECG data on ~2000 subjects exposed to ABT-773. ECG's will be performed pre-, during, and post-therapy. Additionally, the timing of the ECG and the timing of the dose before the ECG will be documented. FDA requested that we amend all informed consents to mention possible effects on cardiac repolarization caused by ABT-773. Various examples of wording was then discussed and we agreed that we would amend the informed consents for all IND studies. Dr. Soreth asked why we were not doing ECG's in the sixth study. Carl stated that the European pharyngitis study would not include ECG's based on recommendations of our European advisors based on the number of existing visits and the likelihood of subject reluctance to participate in a trial for this disease with so many visits. FDA strongly disagreed with this justification. Dr. Murphy expressed concern that we were blatantly misinforming the subjects in that trial by not including a procedure that would monitor a potentially serious adverse event that was being included in all other studies. This issue was left unresolved. Other comments regarding the collection of a blood sample taken at the on-therapy ECG, etc. were made. All issues were addressed in a subsequent written correspondence by FDA (faxed 12/5/00, Abbott response 12/14/00).

Relating to the topic of possible adverse effects on cardiac repolarization, the results of the previously submitted toxicology studies were discussed. Dr. Peters requested additional data in the dog model. The requested study should be a two-week acute study with telemetry and the study can run concurrent with the Phase 3 clinical trials. At this point Reid offered to provide some background information. He indicated that the emetic activity of ABT-773 in the unanesthetized dog limits exposure in this species, leading to our selection of the cynomolgus monkey as the non-rodent model. While the primate did not indicate a risk for QTc prolongation, exposures of 17 times the human C<sub>max</sub> in anesthetized dogs did lead to some prolongation. Owing to differences in protein binding, the dog receives about 3 times the amount of unbound drug than does the human with identical exposures, perhaps expanding our margin of safety. Various proposals for the study were discussed between Reid and Drs. Peters and Osterberg. We committed to sending draft protocols to Dr. Peters for review.

Carl briefly discussed the Phase 2 ECG data. Dr. Soreth informed us that they have begun to ask for special population studies with drugs that show an effect on ECG's. In this case they would be looking at a study in otherwise healthy subjects with underlying cardiovascular disease. She commented that only looking at the effects

of ABT-773 in comparator trials might not be realistic (i.e., cisapride and terfenadine looked safe in the clinic too). Dr. Murphy commented that it is in both of our best interests to get all the information we can to show how to use the drug safely.

The rest of the meeting was spent answering specific questions regarding the four main Phase 3 trials (CAP, ABS, ABECB & pharyngitis). Most of the comments related to minor protocol changes. All of the issues discussed were subsequently provided to Abbott by fax on 12/5/00. Abbott formally responded to the fax in IND 57,836, Serial No. 066, dated 12/14/00.

Action Items:

- Amend Phase 3 informed consents to incorporate statements relating to: possible effects on cardiac repolarization caused by ABT-773, possible interactions with other drugs, and stronger precautions for women of childbearing potential.
- Provide full narratives from Phase 2 studies of all patients who had an adverse event of syncope or elevated liver enzymes.
- Submit draft toxicology protocol(s) for comment prior to initiating the studies.
- Submit results from CAP and ABS dose-selection trials when available.
- Submit draft protocols for the two well-controlled, comparative, pivotal studies for CAP and ABS (to be conducted in 2001) for comment as soon as available.

**PLs' IF**



Jeanne M  
Fox/LAKE/PPRD/ABBOTT

11/28/2000 09:27 AM

To Lawrence E Roebe/LAKE/PPRD/ABBOTT@ABBOTT,  
Jerald J Wenker/LAKE/PPD/ABBOTT@ABBOTT,  
Rosemarie K Waleska/LAKE/PPD/ABBOTT@ABBOTT, Rod  
M Mittag/LAKE/PPD/ABBOTT@ABBOTT, Arthur J  
Higgins/LAKE/PPD/ABBOTT@ABBOTT, Linda J  
Swanson/LAKE/PPRD/ABBOTT@ABBOTT, Mike  
Rubison/LAKE/PPRD/ABBOTT@ABBOTT, Walid  
Awni/LAKE/PPRD/ABBOTT@ABBOTT  
John M Leonard/LAKE/PPRD/ABBOTT@ABBOTT, Carl  
Craft/LAKE/PPRD/ABBOTT@ABBOTT, George  
Aynlian/LAKE/PPRD/ABBOTT@ABBOTT, Reid  
Patterson/LAKE/PPRD/ABBOTT@ABBOTT, David D  
Morris/LAKE/PPRD/ABBOTT@ABBOTT, Jie X  
cc Zhang/LAKE/PPRD/ABBOTT@ABBOTT, Linda E  
Gustavson/LAKE/PPRD/ABBOTT@ABBOTT, Joaquin M  
Valdes/LAKE/PPRD/ABBOTT@ABBOTT, Maria M  
Paris/LAKE/PPRD/ABBOTT@ABBOTT, Carol S  
Meyer/LAKE/PPRD/ABBOTT@ABBOTT, Gregory  
Bosco/LAKE/PPRD/ABBOTT@ABBOTT

bcc

Subject Executive Summary of ABT-773 End-of-Phase 2 Mtg w/  
FDA

Yesterday (11/27) the Abbott people on the CC list met with FDA's Anti-Infective Division for the End-of-Phase 2 meeting on ABT-773. Prior to the meeting we had been placed on clinical hold in a teleconference last Monday (11/20). Following are the high points from yesterday's meeting. Detailed minutes of the meeting will be distributed at a later time.

The meeting was generally successful. FDA stated that we are no longer on clinical hold and may proceed with our Phase 3 trials. They have requested additional toxicology work be done to evaluate QT in dogs, but the study can be done concurrently with Phase 3 and they will consider study design proposals from Abbott. FDA accepted the design for the CAP and sinusitis dose-selection studies, although they suggested changes to the statistical analyses for these studies. While FDA acknowledged that our proposal for 15 resistant isolates/pathogen to support a claim for resistant organisms looked reasonable, they will need a good, solid body of evidence. They cautioned us that they have not seen a body of data that supports macrolide resistant Strep pneumo as a clinical concern. They also advised us that we would need to include bacteremic CAP patients with resistant pathogens in order to secure an indication, which would be difficult to do with an oral drug. The FDA reviewers provided a number of recommended protocol changes, most of which are minor to actual study conduct. In addition, we were directed to modify all of our informed consents to inform patients that QT prolongation has been seen with related classes of drugs and therefore may be a risk with ABT-773.

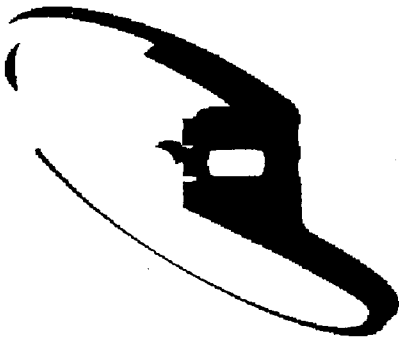
jeanne



CONFIDENTIAL  
ABBT0558150

**PLs' IN**

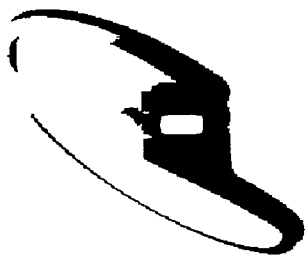




# **ABT-773 Update February 12, 2001**

# Agenda

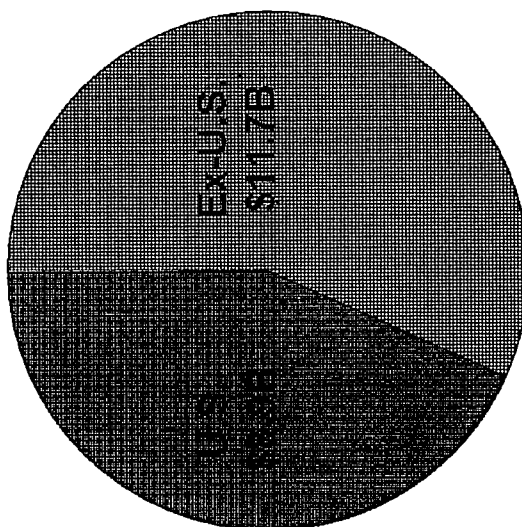
- Introduction
- The molecule
- Phase III tablet program Issues
  - QT
  - Liver Function
  - Dosing
- IV program
- Pediatric program
- Japan program



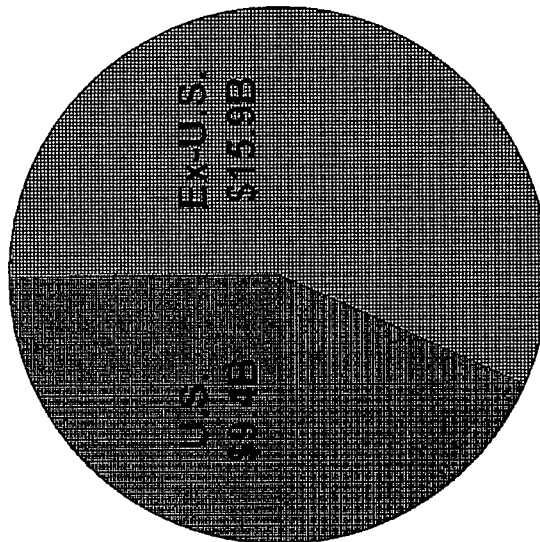


## Global Antibiotic Market Sales Current vs Future Projection

1999 Global Sales \$20.6B



2005 Global Sales \$25.3B



The antibiotic market is a large market and is expected to expand on a global sales basis

# Global Market Drivers

## Negative vs Positive Drivers

### • Antibiotic Resistance

Increasing sensitivity toward “appropriate use” may have negative impact on usage ↓  
Requires new agents to keep ahead of resistant pathogens; substitution of older generic agents with newer branded agents ↑

### • Patent Expirations

May increase price sensitivity and bargaining power of MCOs ↓  
Use of generic agents tend to decrease over time; obsolescence/resistance may further that trend ↑

### • Unmet Need ↓

–Overall unmet need relatively low  
–Cost, convenience, tolerability take on added importance  
–Increasing use of “implied efficacy” metrics i.e. MICs, resistance surveillance, AUC/MIC, MPC, kill kinetics

### • Competition ↓

–6 NDAs/approvals in last 12 months; Avelox, Tequin, Factive, Spectracef, Ketek, Zyvox  
–Continued discovery/development activity by key competitors  
–High level of promotional activity

Negative driver ↓  
Positive driver ↑

# Key Success Factors

## U.S. vs ex-U.S.

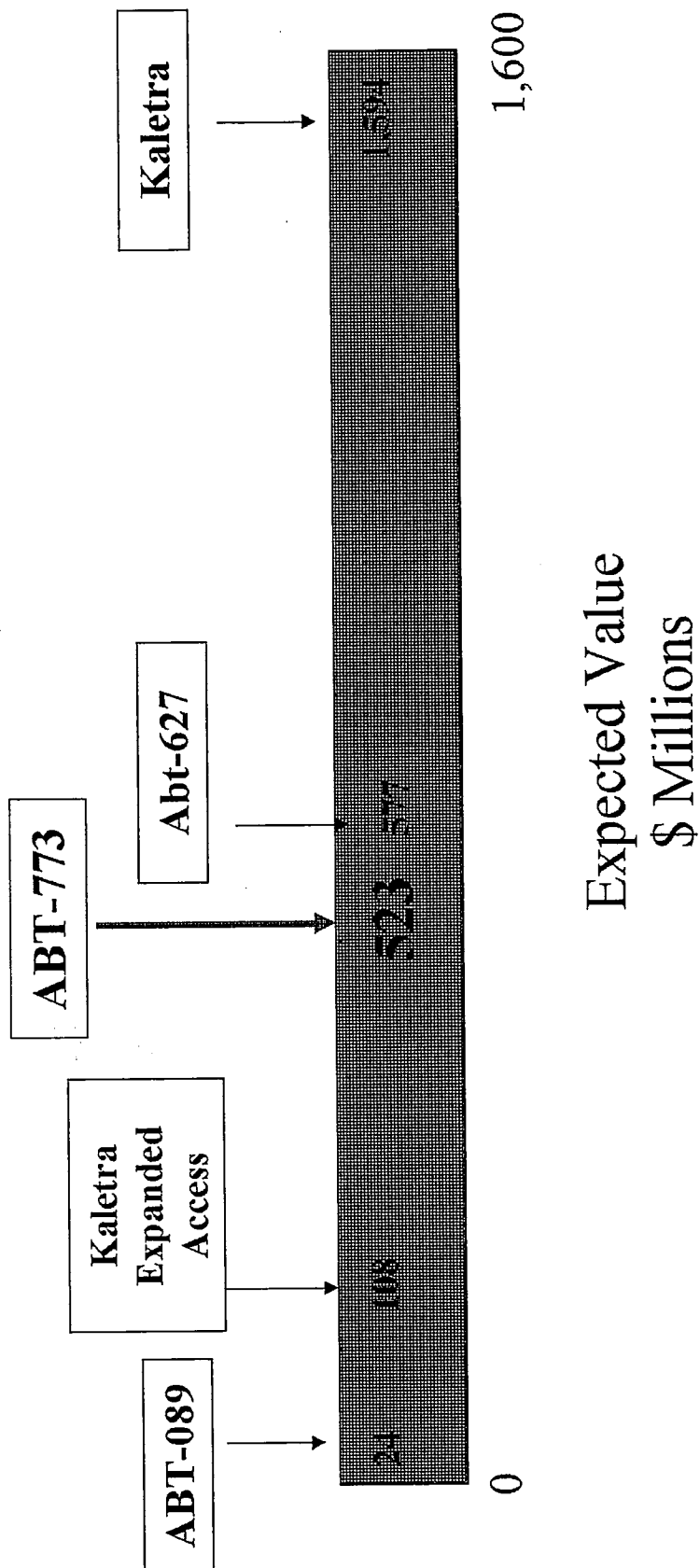
U.S. Assessment			Ex-U.S. Assessment		
Profile	Efficacy	++	Requires a certain baseline level of efficacy across all indications as a "ticket to entry", but is difficult to differentiate agents based on efficacy	+++	While also difficult to differentiate based on efficacy, efficacy takes on added importance with respect to regulatory approval, especially in CAP.
	Tolerability	+++	Success of Zithromax and Levaquin have redefined expectations for tolerability of new agents; agents must offer very good tolerability given numerous alternatives	++	Although important, markets are willing to bear somewhat higher incidence of adverse events, provided they are not severe (i.e. taste perversion); over time, however, AE hurdles will continue to be increased
	Convenience	+++	Zithromax and recent quinolones have moved the market toward short course therapies dosed once daily; Biaxin in 1991 represented the last major BID entrant	++	While in some cases durations are even shorter (azi 3-day AECB), market levies relatively minor penalties for BID dosing
	Resistance Claim	++	Important to leverage the overall ketolide message, and to maximize formulary access, although availability of data may be able to accomplish same end	+++	May prove critical in the regulatory decision of approvability, as well as in setting premium pricing
	Price	+	Able to set price in accordance with optimal price/demand relationship; only moderate price sensitivity in market, though this could increase with increased number of generic competitors over mid-term	+++	Pricing figures heavily into the overall profitability of the compound and is governed by merits of product profile relative to other agents.
Regulatory	Approvability	+	With data showing equivalence to comparators, is not a major area of concern	+++	Will take into consideration PK profile in addition to clinical data, which could weaken argument for approval; given the pivotal nature of CAP approval to overall compound viability, regulatory risk is magnified; will require very strong clinical data if 150 mg OD is to be supported
Profitability	COGS	+	Allows for > 90% SMM given price parity to Zithromax	++	Due to pricing constraints, COGS represents a larger issue; current estimates are 76% SMM at launch rising to 87% peak
	Price	+	Assumes price parity to Zithromax	+++	Profile may limit optimal pricing

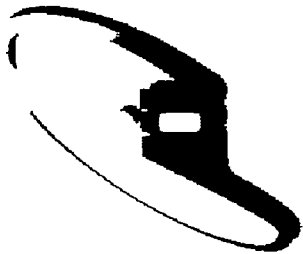
+ Minor Factor

++ Moderate Factor

+++ Major Factor

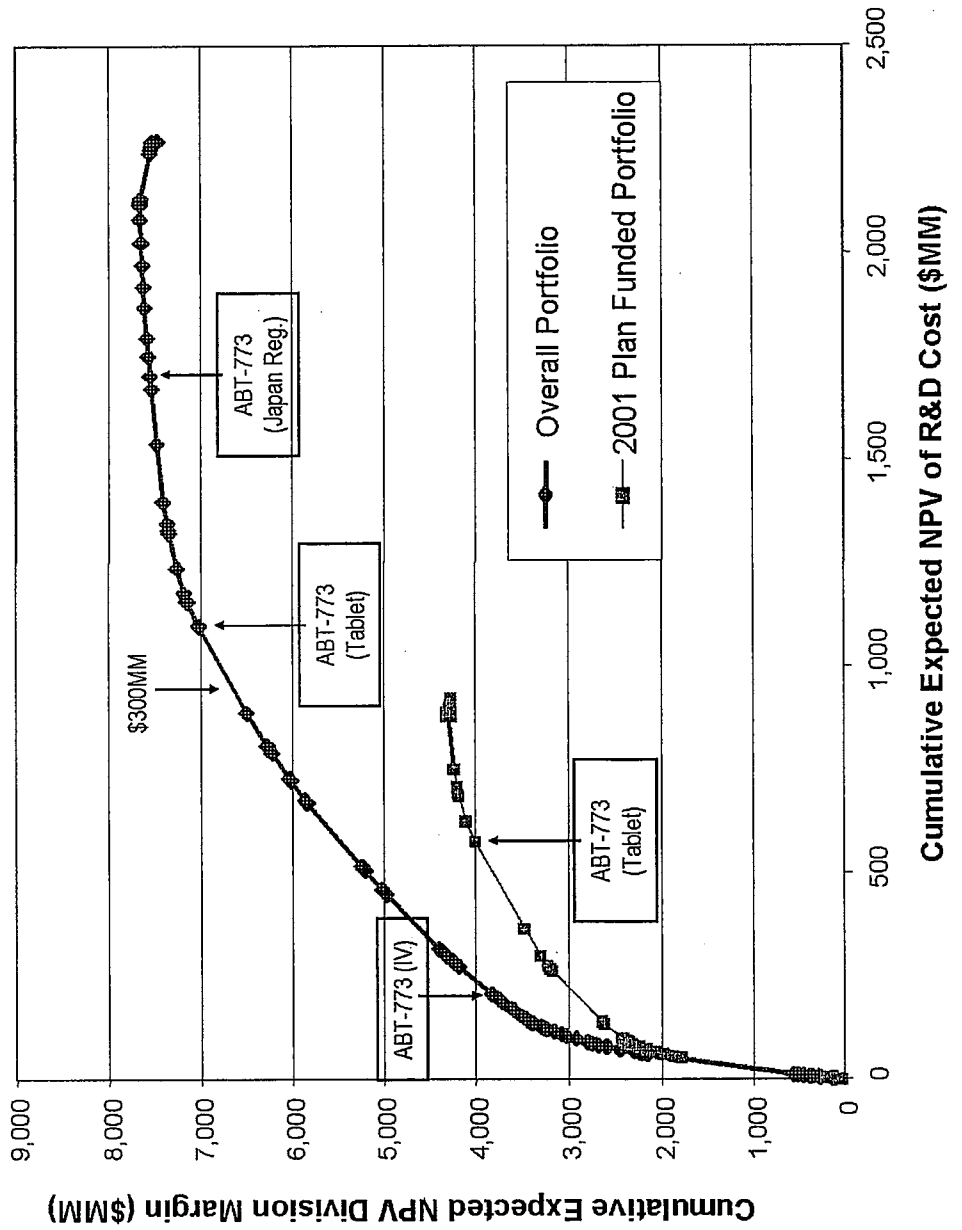
# ***ABT-773 Comparison with other funded projects in 2001 Plan Portfolio***

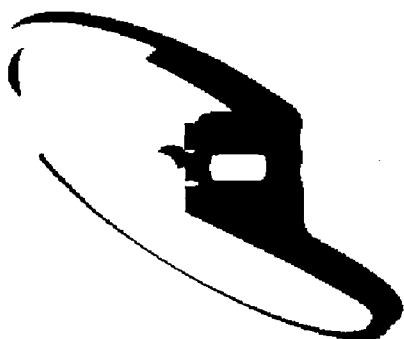




# ***ABT-773 Comparison with other funded projects in 2001 Plan Portfolio***

## **Portfolio Productivity Analysis**



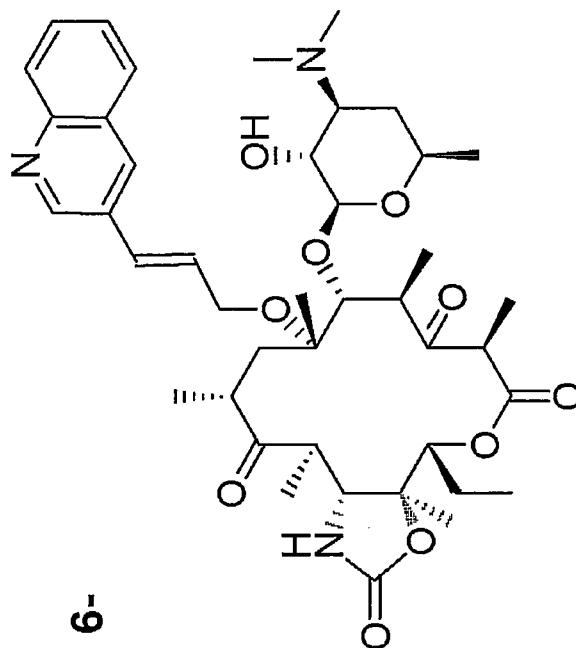


**ABT-773**

**The Molecule**



# ABT-773 Ketolide

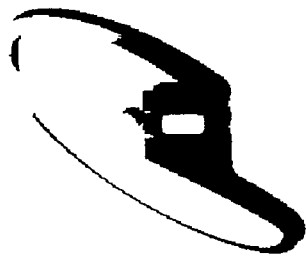


•Quinolylallyl propenyl moiety at the 6-  
0 -position

•Keto group at the 3-position

•Carbamate group at the  
11, 12-position

ABT-773



## ABT-773 Ketolide

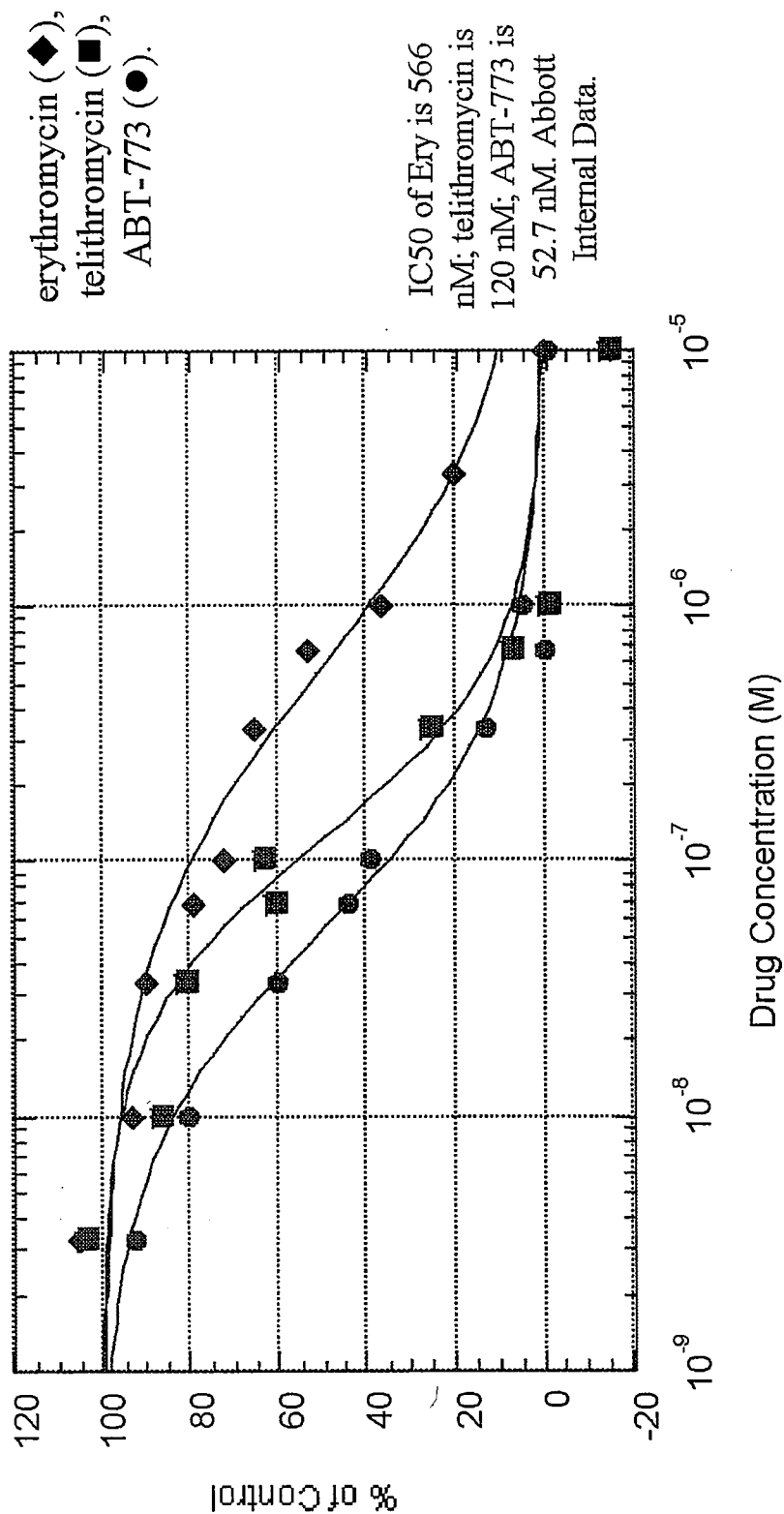
- **Ketolides are a Novel Class of Antimicrobial**
- Active includes key respiratory tract infection pathogens including macrolide and penicillin resistant *S. pneumoniae* and *S. pyogenes*
- Bactericidal activity
- Prolonged post antibiotic effect
- Reduced resistance development

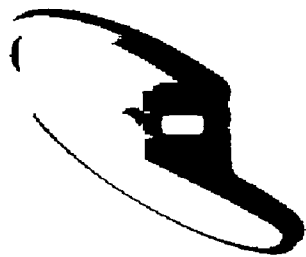
# Microbiology

Organism	MIC <sub>90</sub> $\lambda$ g/ml			
	ABT-773	Ketek	Clari	Azi
<i>S. pneumoniae</i> ery-S	0.008	0.004	0.03	0.12
<i>S. pneumoniae</i> mef	0.12	1.0	4.0	16.0
<i>S. pneumoniae</i> erm	0.01	0.12	>32	>32
<i>S. pyogenes</i> ery-S	0.12	2.0	1.0	2.0
<i>S. pyogenes</i> ery-R	0.5	>8.0	>32	>32
<i>M. catarrhalis</i>	0.25	0.25	0.5	0.25
<i>H. Influenzae</i>	2.0	2.0	16	2.0
Legionella	2.0	2.0	0.06	1.0
<i>M. Pneumoniae</i>	<0.005	<0.005	0.008	<0.005
<i>C. Pneumoniae</i>	0.015	0.06	0.06	0.12

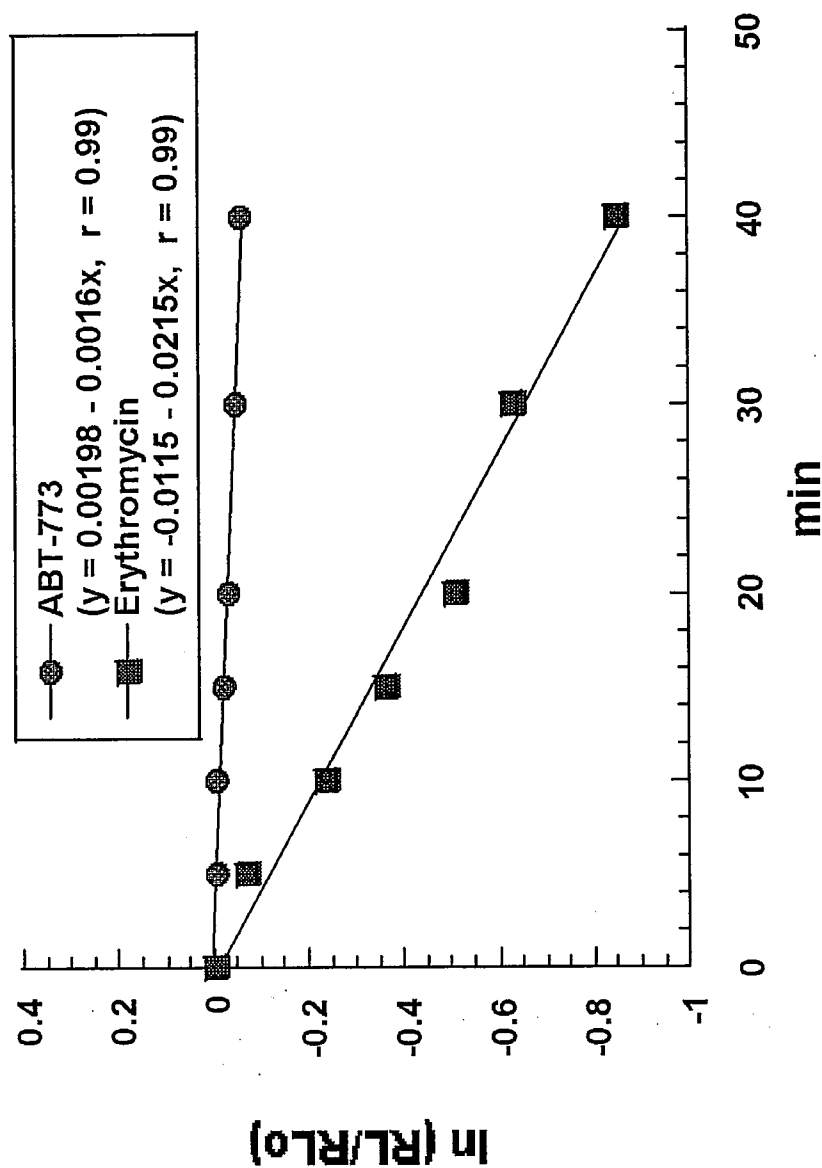


# Ribosome Binding, Susceptible *S. pneumoniae*

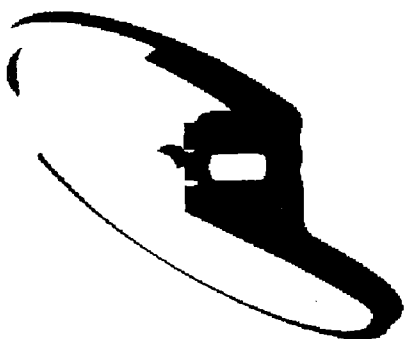




# ABT-773 Displacement in Susceptible *S. pneumoniae* 2486



J. Capobianco et al.  
ICAAC 1999, #2137.



# **QTc potential and Liver Toxicity Issues**

## QTc Prolongation Issues

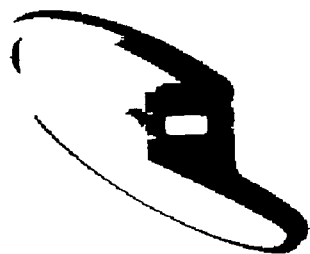
- Potential for QTc Prolongation is a hot button worldwide
  - Antimicrobial agents including macrolides and quinolones are of concern to regulatory agencies
  - ICH guidelines require data from animal models and 200 patients
  - FDA is in the process of evaluating all drug class known to have a potential for prolonging QTc (erythromycin and clarithromycin)
  - FDA has question whether ketolides behave like macrolides
  - FDA requested additional dog tox work to evaluate QTc
  - Required to include ECG monitoring in pivotal Phase 3 studies
  - FDA may require a Phase I study in patients with underlying cardiac disease
  - Some antimicrobials now contain warnings for QT prolongation
  - Telithromycin (Ketek) data residing at FDA
    - Advisory Meeting rescheduled to May 2001 probably not related to QTc concerns





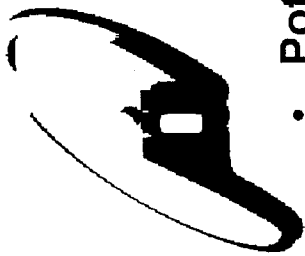
## QT<sub>c</sub> Prolongation Issues ABT-773

- Pre-clinical data positive for QT<sub>c</sub> dose response.
- A possible dose effect in Phase I at total daily dose  $\geq 800$  mg.
- No significant QT effect observed when ABT-773 was administered with the metabolic inhibitor ketoconazole. (Increased ABT-773 C<sub>max</sub> 5X)
- No concentration response in Phase I studies ( $\leq 300$ mg).
- No consistent QT effect observed at clinical doses studied in Phase IIB studies. (150 mg QD to 600 mg QD)



## **QT<sub>c</sub> Prolongation Issues ABT-773 Plan**

- Completed pre-clinical evaluation of ABT-773
- Completed ECG monitoring of >200 patients in Phase II and III
- Continue to monitor QTc and electrolytes in Phase III programs.
- Planning FDA requested study of QTc in patients with pre-existing cardiac disease.
- IV ABT-773 Phase I study will monitor QTc carefully
- Consult with Drs. Morganroth and Moss QTc advisors.



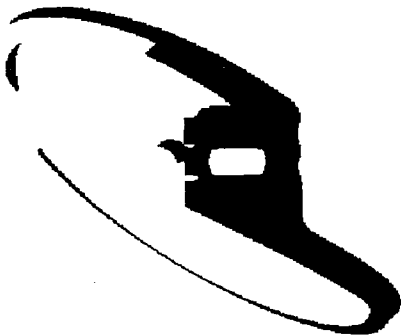
## Liver Toxicity Issues

- Potential for liver toxicity is a concern for the FDA
  - Recent liver toxicity seen with Trovofloxacin are of concern to regulatory agencies.
  - Gemifloxacin recently not approved by FDA because of liver toxicity concerns.
  - FDA meeting on guides to industry on how to study liver function scheduled for February 11-12, 2001



## **Liver Toxicity Issues for ABT-773**

- Preclinical tox showed some effect on the liver function.
- Japanese in bridging study showed increased LFTs.
- No evidence of LFT issue in Western subjects.
- No evidence of dose response.
- Repeat of Japanese bridging study in Japan showed No evidence of LFT increases in Japanese or Caucasians.
- ABT-773 plan for accessing problem
  - Continue to monitor LFT in Phase III programs.
  - Jean Fox will attend FDA meeting.



# Phase III Program

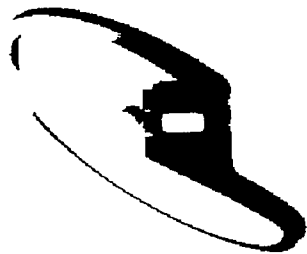
# Phase III Program

## Proposed Indications and Treatment Duration

Infection	Dosage	Duration
Pharyngitis/Tonsillitis due to: <i>S. pyogenes</i> *	150 mg QD	5 d
Acute bacterial sinusitis due to:		
<i>H. influenzae</i>	150 mg QD or BID	10 d
<i>M. catarrhalis</i>	150 mg QD or BID	10 d
<i>S. pneumoniae</i> **	150 mg QD or BID	10 d
Acute bacterial exacerbation of chronic bronchitis due to:		
<i>H. influenzae</i>	150 mg	5 d
<i>H. parainfluenzae</i>	150 mg	5 d
<i>M. catarrhalis</i>	150 mg	5 d
<i>S. pneumoniae</i> **	150 mg	5 d
Community-acquired pneumonia due to:		
<i>C. pneumoniae</i>	150 mg QD or BID	10 d
<i>H. influenzae</i>	150 mg QD or BID	10 d
<i>L. pneumophila</i>	150 mg QD or BID	10 d
<i>M. pneumoniae</i>	150 mg QD or BID	10 d
<i>S. pneumoniae</i> **	150 mg QD or BID	10 d

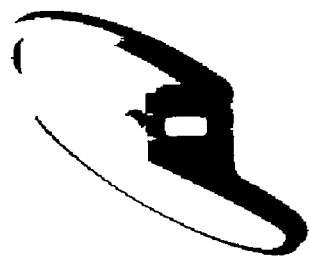
\* Including macrolide-resistant strains.

\*\* Including penicillin-resistant and macrolide-resistant strains.



## **Phase III Program Studies Started in Year 2000**

<b>Study</b>	<b>Indication</b>	<b>ABT-773 Regimen</b>	<b>Comparator</b>	<b>Number Subjects</b>	<b>Location</b>
M00-223	Pharyngitis	150 mg QD 5 days	Penicillin V	185/520	US (IND)
M00-222	Pharyngitis	150 mg QD 5 days	Penicillin V	0/520	EU (Non-IND)
M00-216	ABECB	150 mg QD 5 days	Azithromycin	131/600	US, Canada IND
M00-217	ABECB	150 mg QD 5 days	Levofloxacin	0/500	EU (Non-IND)



## Phase III Program Studies Started in Year 2000, Con't

### Dose Finding Studies for Sinusitis/CAP:

Study	Indication	ABT-773 Regimen	Comparator	Number Subjects	Location
M00-225	Sinusitis	150 mg QD vs. 150 mg BID 10 days	None	137/500	US, EU (IND)
M00-219	CAP	150 mg QD vs. 150 mg BID 10 days	None	76/500	US, Canada, EU (IND)



# SDG Analysis of Ph. III CAP Development Options

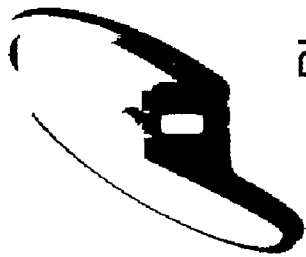
CAP Development Strategy	Timeline impact	Incremental Cost	Relative Regulatory Risk	Potential for 150 mg. QD in CAP
1. 150 mg QD only Ph. III (Begin now)	8/2002	0	High	Yes
2. Further Phase II 150x dose ranging, then Phase III	Significant delay (~1 year)	\$5.4M	Low	Yes
3. Parallel Phase III program for 150 mg QD/150 mg BID	Significant delay (~1 year)	\$24.3M	Low	Yes
4. 150 mg BID only Ph. III (Begin now)	8/2002	0	Mod	No
5. 300 mg QD only Ph. III (Begin now)	8/2002	0	Low	No
6. Phase III open-label dose ranging	8/2002	\$7.2M	Low	Yes

Selected Strategy

Positive Factor

Neutral Factor

Negative Factor



# Dosing Issue

## 150 mg BID vs 150 mg QD: Background

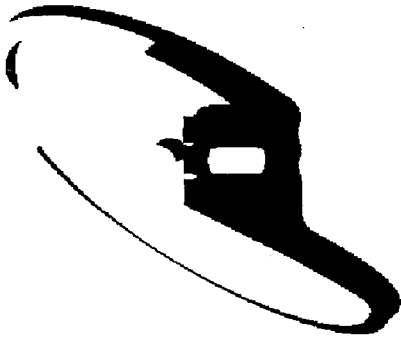
- Phase II data indicated 300 mg QD was not viable due to high levels of diarrhea (10-20%) and taste perversion (10-20%)
- Phase II ABECB and pharyngitis/tonsillitis data supported 150 mg QD
  - 150 mg QD currently being evaluated in ongoing phase III trials in these indications
- Dosing selection for CAP and sinusitis confounded by limited data
  - few bacterial isolates, particularly with H. flu, in sinusitis
  - no 150 mg arm in CAP trial
- To increase probability of correct dose selection in CAP/sinusitis, additional studies are ongoing to generate more data in these indications
  - 150 mg QD vs 150 mg BID CAP & sinusitis trials ongoing



# Dosing Issue

## 150 mg BID vs 150 mg QD: Implications of Decision

- Regulatory and commercial environments differ dramatically between U.S. and ex-U.S.
  - For U.S., market:
    - Absence of consistent QD dosing for all indications represents a significant commercial hurdle
    - Approval on indication-by-indication basis
    - Optimal strategy for U.S. may be to pursue QD dosing for CAP/sinusitis
  - For ex-U.S. market:
    - CAP data represents the “lynchpin” for approvability of the entire molecule, hence a conservative BID approach may result in lower regulatory/commercial risk
    - Relatively minor commercial impact of BID dosing
    - Optimal strategy for ex-U.S. may be to pursue BID dosing for CAP and perhaps sinusitis
- A decision of 150 mg QD vs 150 mg BID in CAP & sinusitis will be made based on phase III data 2Q01
  - Data may not show a clear “winner” due to relatively low power of studies; may be a difficult decision
  - Due to soft global flu season and protocol amendments, enrollment is behind plan and could impact timing of decision
- A plan to have divergent US/Ex-US clinical programs in CAP/sinusitis may be required to minimize regulatory / commercial risks
  - Cost / timeline implications



# ABT-773 IV Program

# Once-daily Zithromax® I.V. (azithromycin for injection)

The only I.V. advanced-generation  
macrolide for community-acquired  
pneumonia\* in adult hospitalized patients

Targeted coverage of the key pathogens of  
community-acquired pneumonia

Typical	Atypical
<i>Streptococcus pneumoniae</i>	<i>Legionella pneumophila</i>
<i>Haemophilus influenzae</i>	<i>Chlamydia pneumoniae</i>
<i>Staphylococcus aureus</i>	<i>Mycoplasma pneumoniae</i>
<i>Moraxella catarrhalis</i>	

Proven as effective as  
cefuroxime ± erythromycin

Early step-down therapy to oral Zithromax  
Very well tolerated

The most common side effects associated with treatment in adult patients who received IV/PO Zithromax in studies of community-acquired pneumonia were diarrhea (1.3%), nausea (1.3%), rash (1.3%), abdominal pain (2.7%), and vomiting (1.1%). The most common side effects related to infusion or injection pain at the site of infusion (6.1%) and oral inflammation (3.1%).

Zithromax is contraindicated in patients with known hypersensitivity to azithromycin, erythromycin, or any macrolide antibiotic.

Once-daily  
**Zithromax I.V.**  
azithromycin for injection  
by prescription

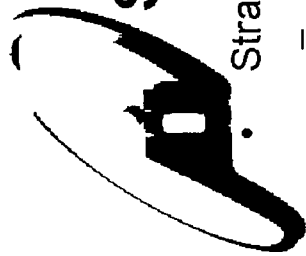
The Power of Z in I.V.

The Power of  
Z  
in I.V.

\*Zithromax I.V. is indicated for community-acquired pneumonia due to *Chlamydia pneumoniae*, *Haemophilus influenzae*, *Legionella pneumophila*, *Moraxella catarrhalis*, *Mycoplasma pneumoniae*, *Staphylococcus aureus*, or *Streptococcus pneumoniae* in patients who require intravenous therapy.

In a controlled study of 281 hospitalized patients with community-acquired pneumonia, patients received 1000 mg single daily dose by the intravenous route for 2 to 5 days, followed by 500 mg daily by the oral route to complete 7 to 10 days of therapy. This was compared with cefuroxime (250 mg daily in three divided doses by the intravenous route for 2 to 5 days followed by 1000 mg daily in two divided doses by the oral route to complete 7 to 10 days of therapy), with or without erythromycin.

Please see brief summary of prescribing information on last page of this advertisement.



# ABT-773 IV Formulation

## Strategic, Commercial, and Technical Value

### Strategic Value

- IV represents a channel not currently served by Anti-infective Franchise
- Leverages presence of Medical Center Reps and experience with ID community

### Commercial Value

- IV availability figures favorably into decisions regarding formulary access to molecule
  - potential advantage over telithromycin, which will not have an IV
  - required to compete effectively with Zithromax, Tequin, Avelox which have IVs
- Positive impact on tablet formulation
  - estimated \$36MM incremental to peak tablet sales due to step-down therapy
  - Enhances overall “potency” image of brand

### Technical Value

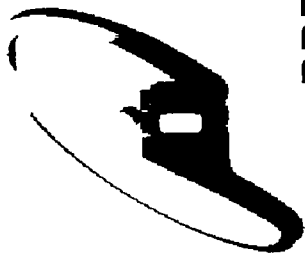
- Support for *S. pneumoniae* Resistance claim
  - FDA indicated that bacteremic patients will be important to establish body of evidence for this claim
- Provides additional information on QT effects

IV launch currently lags tablet launch by 1 year; any further delays will reduce the potential value



## **ABT-773 IV Program Formulation Objectives**

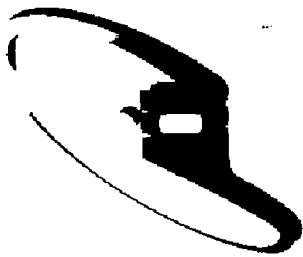
- Reconstituted solution . Once a day dosing. Low pain on injection
- Lyophilized powder, consisting of ABT-773 and a counter ion base.
- One strength, in a flip-top vial and the ADD Vantage system at launch.
- Diluent volume 100ML, with length of infusion (30 to 60 minutes) and type of diluent (Dextrose 5% and/or normal saline) TBD based on animal pain models, clinical and stability studies.



## **ABT-773 IV Formulation PPD/HPD Funding Status**

- PPD/HPD Collaboration initiated 9/99
- PPD funded Program 01/00-08/00 (\$1.4MM)
  - Formulation development ( lactate salt, lyophilized powder)
  - Animal pain models
  - Two week Tox study (monkey)
- HPD funded Program 08/00-12/00 (\$0.8MM)
  - Two week Tox study (rat)
  - Clinical supplies for Phase I
  - Stability program
- 2001 funding
  - HPD first pass funding cut for 773 IV (\$7MM)
  - Milestone funding to Phase I Go/No Go (\$1MM)
- Total program development costs 2000 - 2003 (\$22.5MM)

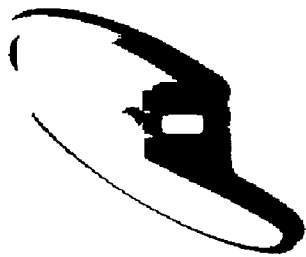




## **ABT-773 IV Formulation**

### ***Animal Pain Study Results***

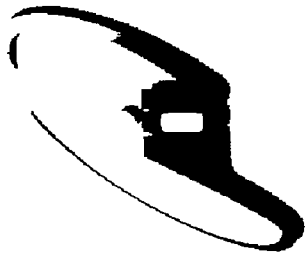
- Assessed 6 prototypes (3 different counter ions at 2 pH levels) vs clarithromycin IV and azithromycin IV
- Animal pain models showed no differentiation among all three compounds
  - Results not conclusive
  - Need to evaluate in humans
- Chose ABT-773 lactate as the prototype to test in Phase I studies based on manufacturability and stability.



## **ABT-773 IV Planned Clinical Program**

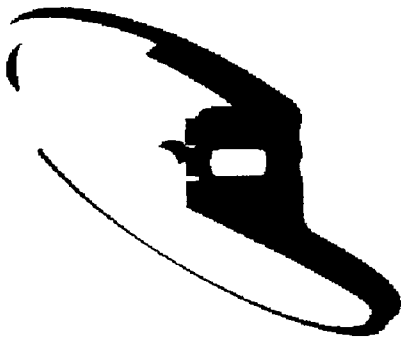
*With 2001 funding decision in Feb:*

- |  |         |
|--|---------|
| • Single Dose-rising Phase I study         | Apr/01  |
| • Multiple Dose Phase I with selected dose | June/01 |
| • File US IND                              | Oct/01  |
| • Initiate Phase III                       | Dec/01  |
| – 2 step-down CAP studies (US/Europe)      |         |
| – 2-3 days dosing                          |         |
| – Two seasons to complete                  |         |
| • Filing                                   | Aug/03  |

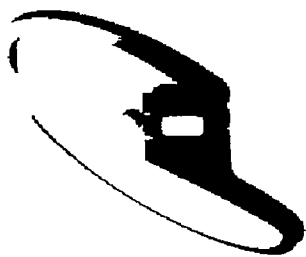


## ABT 773 IV Program Summary

- **Comments**
  - Funding for '01 not available PPD/HPD
  - Go/No go could be made after Phase I based on safety profile (pain, QT, GI)
  - Milestone funding recommended (\$1MM)
  - Assuming Go, '01 budget estimated \$7MM
  - IV will help to obtain resistant *S. pneumo* claim
  - Total Program Cost 2000-2003 (\$22.5MM)



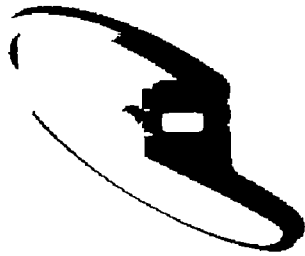
# Pediatric Program



# **ABT-773 Pediatric Formulation**

## **Importance to the 773 program**

- Increased perception of safety
- Better pricing and acceptance in European markets
- FDA requires studies in pediatrics



## **ABT-773 Pediatric Program Formulation Objectives**

- Develop coated particle formulae for global use
  - coated particles for Suspension - 150mg/5mL & 300mg/5mL
  - coated particles as a dry syrup, sprinkle or sachet.
- Desired Properties
  - Once a Day Dosing
  - Acceptable 'Initial Taste'
  - Minimal 'After Taste'
  - No Unpleasant Mouth-feel
  - Acceptable Color and Flavor
  - No Refrigeration Required.

# ABT 773 Pediatric Program

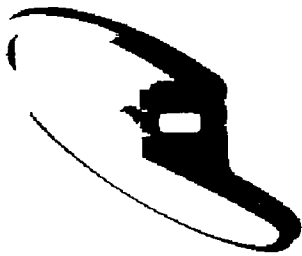
## Taste Assessment

### Sensory Analysis of Uncoated Drugs Summary of Results

The three drug substances can be ranked from most to least bitter as follows:

Drug Substance	Concentration (ppm) Which Exhibits an Initial Bitter Intensity $\leq 1$ (Slight)
ABT-773	0.79
Clarithromycin	4.2
Azithromycin	15

- ABT-773 is approximately five times more bitter than clarithromycin

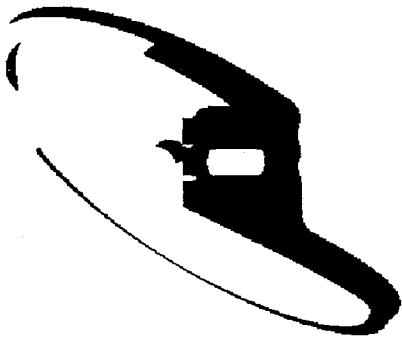


## **ABT 773 Pediatric Program**

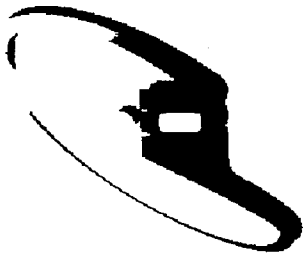
### ***Taste Assessment***

- The ABT-773 encapsulated prototype #2 may be at risk of dosing compliance problems due to flavor quality.
- Overall ABT-773 Prototype 2
  - Less bitter than Biaxin both initial and after taste
  - More bitter than Zithromax both initial and after taste
- For ABT-773 Prototype 2, the flavoring aromatics and sweetness decay quickly, exposing the bitterness which lingers throughout the aftertaste at or above the “concern” intensity level.



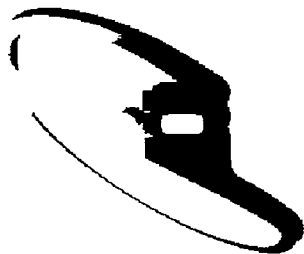


# Japan Program



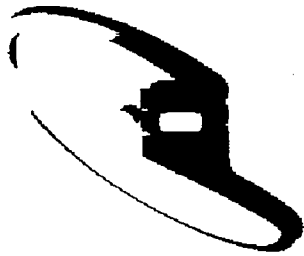
## Japan Program Taisho

- Japan development is planned in coordination with Taisho and Dainabot
- Meetings are held at least 3 times a year to review developments
- Taisho funds 10.69% of global development costs and 50% of local Japan costs.
- Bridging strategy is primary plan for development in Japan



## Japan Program Clinical Plan

• Phase I in Japan	<u>Start</u>
– Food Effect Study	Completed
– Single and multiple dose study	Completed
– Review data (Abbott/Taisho)	April/01
• PK data Japanese vs Caucasian	
• Development program strategy	
– Present Kiko data and recommend development program May/01	
– Start Tissue Conc. Study	2Q/01



## Japan Program Clinical Plan

- PK similar in Japanese and Caucasians (12/02 filing)
  - Recommend to Kiko same dose in Japan as in ex-Japan
  - Recommend to Kiko one comparative bridging study in CAP (Phase III) and several smaller local studies in skin infections, dentistry, otolaryngology, UTI and pan-bronchiolitis
  - Taisho agreement necessary prior to Kiko meeting
- PK different in Japanese and Caucasians (12/03 filing)
  - Phase II dose ranging study in CAP (Bridging study)
  - Phase III comparative study will be required
  - Full development time line
  - Implications on Taisho cost-sharing

**PLs' IO**

## ABT-773 Update February 12, 2001

**Introduction**

ABT-773 is a ketolide antimicrobial, an evolutionary step from the macrolide antimicrobials such as erythromycin and the new generation macrolides like clarithromycin and azithromycin. It is in phase III development as a replacement to clarithromycin.

The antibiotic market is a large market (\$20.5 Billion in 1999) and is expected to expand on a global sales basis (\$26.5 Billion in 2005). The majority of the markets sales are in the oral tablet/capsule segment. Market sales increases are being driven by replacement of older/cheaper agents with branded agents. Zithromax has driven market demand for cost/convenience/tolerability, while the quinolones (Levaquin, Tequin, Avelox) are the fastest growing segment, playing into resistance concerns. Resistance is a major driving force for both the quinolones and ketolides development.

**Ketolides are a Novel Class of Antimicrobial**

- Active includes key respiratory tract infection pathogens including macrolide and penicillin resistant *S. pneumoniae* and *S. pyogenes*
- Bactericidal activity
- Prolonged post antibiotic effect
- Reduced resistance development

ABT-773 is the most active ketolide presently under development. It is 5 to 10 times more active than telithromycin (Aventis ketolide) against *S. pneumoniae* and *S. pyogenes* including resistant strains. It has equal activity to telithromycin and azithromycin against *H. influenzae*. The increased activity can be attributed increased ribosomal binding. Compared to macrolides that bind only to domain V, ABT-773 binds to both domains II and V. The binding is essentially irreversible and provides bactericidal activity against *S. pneumoniae*.

**Key issues facing the ABT-773 development program are summarized below**

**QTc Issues**

The potential for QTc prolongation is currently a prominent issue facing drug development across therapeutic areas-worldwide. Antimicrobial agents including macrolides and quinolones are of concern to regulatory agencies. There is considerable scientific uncertainty in relating the findings from in vitro assays and animal models to clinical risk of malignant arrhythmias. In an effort to gain more

Confidential

ABBT205042

*Leiden* EXHIBIT *44*  
 FOR I.D. *4-26-07* *[Signature]*

knowledge these agencies are requiring the pharmaceutical companies to do additional test including

- ICH guidelines require data from animal models and 200 patients
- FDA is in the process of evaluating all drug class known to have a potential for prolonging QTc (erythromycin and clarithromycin)
- FDA has question whether ketolides behave like macrolides
- FDA requested additional dog tox work to evaluate QTc of ABT-773
- ABT-773 studies required including ECG monitoring in pivotal Phase 3 studies.
- FDA may require a Phase I study in patients with underlying cardiac disease, but the design for these studies has not been determined.
- Some antimicrobials now contain warnings for QT prolongation such as moxifloxacin.
- Telithromycin (Ketek) data residing at FDA will be reviewed by FDA Advisory Committee at a meeting scheduled for May 2001 probably related to concerns about efficacy and not related to QTc concerns.

The ketolide ABT-773 will be considered guilty until proven innocent because it is related to erythromycin and clarithromycin which are also suspect and under scrutiny. ABT-773 has the following data related to its potential or lack of potential to affect the QT interval.

- Preclinical data positive for QTc dose response.
- A possible dose effect in Phase I at total daily dose  $\geq 800$  mg.
- No significant QT effect observed when ABT-773 was administered with the metabolic inhibitor ketoconazole. (Increased ABT-773 Cmax 5X)
- No concentration response in Phase I studies ( $<300$ mg).
- No consistent QT effect observed at clinical doses studied in Phase IIB studies. (150 mg QD to 600 mg QD)

The Venture plan for dealing with the uncertainties related to developing a drug which has an unknown potential for prolonging the QT intervals is to pro-actively attempt to find out as much about our drug and the science related to QTc by;

- Completed preclinical evaluation of ABT-773
- Initiate FDA recommended dog studies.
- Completed ECG monitoring of  $>200$  patients in Phase II and III
- Continue to monitor QTc and electrolytes in Phase III programs.
- Perform FDA requested study of QTc in patients with pre-existing cardiac disease; perform phase I study as required by CPMP.
- IV ABT-773 Phase I study will monitor QTc carefully
- Consult with Drs. Morganroth and Moss QTc advisors.

#### Liver Toxicity Issues

The FDA has similar concerns regarding the potential for liver toxicity of new drugs as it has for QTc issues, since both of these problems have resulted in

drugs being removed from the market shortly after approval. The concerns have been directed at the quinolones, but all antimicrobials are under going extensive evaluations. The FDA has a meeting on guidance to industry on how to study the potential for liver toxicity, scheduled for February 11-12, 2001. Jean Fox will attend this meeting and report back on it so that we will be able to update this topic at the February meeting.

In the Japanese bridging study run in Hawaii we saw increases in LFTs in Japanese subjects. This was very disturbing, since increases in LFTs were seen only in the Japanese subjects. In addition the Japanese subjects had AUCs which were 50% higher than the western subjects. LFTs in over 1000 western subjects did not show any problems. Since, the Japanese subjects with elevated LFTs did not show a dose response, it was felt that the changes in LFTs might be related to the high caloric diet on the unit. To answer this question Phase I food interaction and a repeat of the bridging study was preformed in Japan. The results of this study showed no evidence of any problem with LFTs in the Japanese or Caucasians. Based on the encouraging results we will continue moving forward with the Japan Program.

#### **Phase III Tablet Program**

The Phase III tablet program is underway after several delays related to manufacturing of the 150 mg tablet to replace the 300 mg tablets and the late date (11/27/00) of the FDA End of Phase II meeting. The present plan is to complete the Phase III 150 mg once daily indications in the US and Europe this year. These studies include two pharyngitis studies compared to penicillin 500 mg TID, one ABECB study in the US compared to Azithromycin, and one European ABECB study compared to Levofloxacin. The CAP and sinusitis dose selections studies are running globally, but no European sites are enrolling yet due to the changes in the protocol following the FDA End of Phase II meeting. We are increasing sites and planning to go to the Southern Hemisphere if needed to complete the studies before the start of the fall respiratory season. These changes have added additional costs that will add approximately \$5.0 MM to the budget.

The results of the CAP and Sinusitis studies have the potential of generating divergent development paths based on differences in AI and PPD regulatory and commercial considerations. PPD would prefer to have 150 mg once daily for all indications and AI would prefer 150 mg once daily for pharyngitis and ABECB and 150 mg BID for CAP and sinusitis. Once we complete the study we will need to meet to iron out the possible options.

#### **ABT-773 IV Formulation Program**



The IV formulation program is presently unfunded. The IV program is important to overall program because of the following;

- Hospital formulary acceptance
- XX% share gain in Tab sales due to step-down therapy
- Positions 773 for serious infections
- Support for *S. pneumoniae* resistance claim
  - FDA indicated that bacteremic patients will be important to establish body of evidence for this claim
- Provide additional information on QTc effects

The ABT-773 IV program received partial funding last year both from PPD and HPD, but has not been funded for 2001. The following outlines the IV program fund and funding needed.

- PPD/HPD Collaboration initiated 9/99
- PPD funded Program 01/00-08/00 (\$1.4MM)
  - Formulation development (lactate salt, lyophilized powder)
  - Animal pain models
  - Two week Tox study (monkey)
- HPD funded Program 08/00-12/00 (\$0.8MM)
  - Two week Tox study (rat)
  - Clinical supplies for Phase I
  - Stability program
- 2001 funding
  - HPD first pass funding cut for 773 IV (\$7MM)
  - Milestone funding to Phase I Go/No Go (\$1MM)
- Total program development costs 2000 - 2003 (\$22.5MM)

The clinical program with 2001 funding decision in February will included;

- |  |         |
|--|---------|
| • Single Dose-rising Phase I study         | Apr/01  |
| • Multiple Dose Phase I with selected dose | June/01 |
| • File US IND                              | Oct/01  |
| • Initiate Phase III                       | Dec/01  |
| – 2 step-down CAP studies (US/Europe)      |         |
| – 2-3 days dosing                          |         |
| – Two seasons to complete                  |         |
| • Filing                                   | Aug/03  |

The Venture would recommend funding the Phase I study to determine safety and tolerability profile as a GO/No Go decision. Assuming a GO decision we would need \$7 MM 2001 to start Phase III program.

#### **Pediatric Program**

The pediatric suspension program is on hold. ABT-773 is 5 to 7 times more bitter than clarithromycin. This will make the development of an acceptable formulation very difficult. The first prototype tested had a taste that was better than clarithromycin but not as good as azithromycin. The pharmacokinetics showed AUCs that were only 70% of the tablet formulation. Even with the difficulties of making an acceptable formulation the pediatric formulation would have benefits including increasing the perception of safety, better pricing and acceptance in European markets, and FDA requires studies in pediatrics. The Venture would recommend continuing the hold until we resolve other issues and then re-evaluate possible ways of overcoming the taste problem.

#### **Japan Development Program**

The Japan development program is planned in coordination with Taisho and Dainabot. Taisho funds 10.69% of global development costs and 50% of local Japan costs. The Venture is attempting to use a bridging strategy as the primary plan for development in Japan. The Phase I studies in Japan which were initiated in response to the LFT problems in the first bridging study, have been completed. There were not increases in the LFTs of the Japanese or Caucasians in the study. We will be meeting with Taisho and Dainabot to formulate a plan to present to Kiko in the 2<sup>nd</sup> or 3<sup>rd</sup> Quarter.

**PLs' IP**

ABBT205047

# ABT-773 Update February 12, 2001

Confidential

*Leadem* EXHIBIT *45*  
FOR I.D. *4-26-07* *1 gax*

ABBT205048

# Agenda

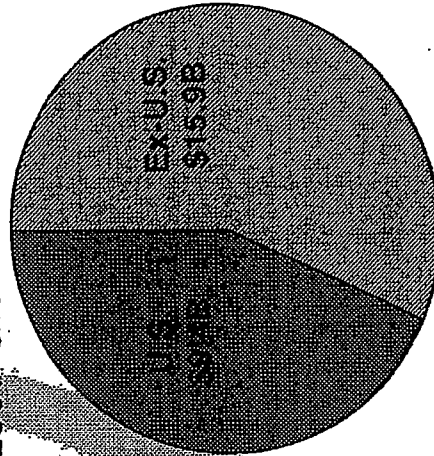
- Introduction
- The molecule
- Phase III tablet program Issues
  - QT
  - Liver Function
  - Dosing
- IV program
- Pediatric program
- Japan program

Confidential

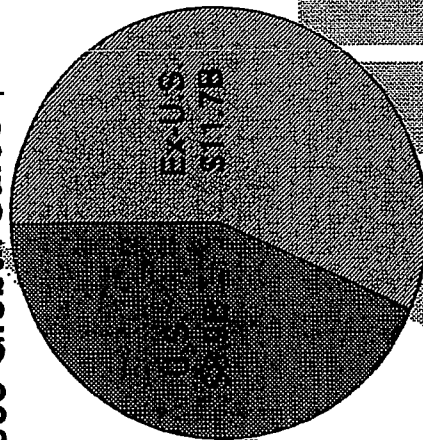
ABBT205049

## Global Antibiotic Market Sales Current vs Future Projection

2005 Global Sales \$25.3B



1999 Global Sales \$20.6B



The antibiotic market is a large market and is expected to expand on a global sales basis

Confidential



ABBT205050

# Global Market Drivers

## Negative vs Positive Drivers

### • Antibiotic Resistance

Increasing sensitivity toward "appropriate use" may have negative impact on usage ↓  
 Requires new agents to keep ahead of resistant pathogens; substitution of older generic agents with newer branded agents ↑

### • Patent Expirations

May increase price sensitivity and bargaining power of MCOs ↓  
 Use of generic agents tend to decrease over time; obsolescence/resistance may further that trend ↓

### • Market expansion ex-US ↑

### • Unmet Need ↓

—Overall unmet need relatively low  
 —Cost, convenience, tolerability, take on added importance  
 —Increasing use of implied efficacy metrics i.e. MICs, resistance surveillance, AUC/MIC, MPC, kill kinetics

### • Competition ↓

—6 NDAs approvals in last 12 months; Avalex, Tigeclin, Factive, Spectracef, Ketek, Zyvox  
 —Continued discovery/development activity by key competitors  
 —High level of promotional activity

↓ Negative driver  
 ↑ Positive driver

Confidential

# Key Success Factors

## U.S. vs ex-U.S.

	U.S. Assessment	Ex-U.S. Assessment
Profile	Efficacy ++ Requires a certain baseline level of efficacy across all indications as a "ticket to entry," but is difficult to differentiate agents based on efficacy.	++ While also difficult to differentiate based on efficacy, efficacy factors are of increased importance with respect to regulatory approval, especially in CDE.
	Tolerability +++ Expectations for tolerability of new agents/agents must differ very good tolerability given numerous alternatives.	++ Although important, markets are willing to deal somewhat higher incidence of adverse events, provided they are not severe (i.e., taste/pain/nausea, etc.). However, AE burden will continue to be increased.
	Convenience +++ Zimmax and recent competitors have moved the market forward. Short course therapies does not exist. Block in HbA1c (part of the last in the B10 family).	++ While in some cases tolerability is even shorter (e.g., 3-day AE/CB), market favors relatively minor penalties for B10 (e.g., 300mg).
	Resistance ++ Important to strength the overall ketamine message and to minimize regulatory concern, although availability of data may be able to accommodate same.	++ Key areas called in the regulatory exclusion of approvability as well as in setting premium pricing.
	Price + Ability to set price in accordance with optimal therapeutic relationship only moderate price sensitivity in market. Though this could increase with increased number of generic competitors over time.	++ Pricing factors heavily into the overall profitability of the compound and is governed by merits of proposed profile relative to other agents.
Regulatory	Approvability + With data showing equivalence to comparators, it is a major area of concern.	++ Will take into consideration PK profile in addition to clinical data, which could weaken argument for approval given the critical nature of OAP approval to overall compound viability. Regulatory risk is magnified, will require very strong clinical data (e.g., 150 mg OD, 150 mg BID, etc.) to be supported.
Profitability	COGS + Allow for + 80% SMM given price parity to Zimmax.	++ Due to ongoing constraints, COGS represents a major threat. Current estimates are 75% SMM at launch, rising to 87% post-launch.
	Pricing + Assumes price parity to Zimmax.	++ Pricing may not optimize pricing.

+ Minor Factor

++ Moderate Factor

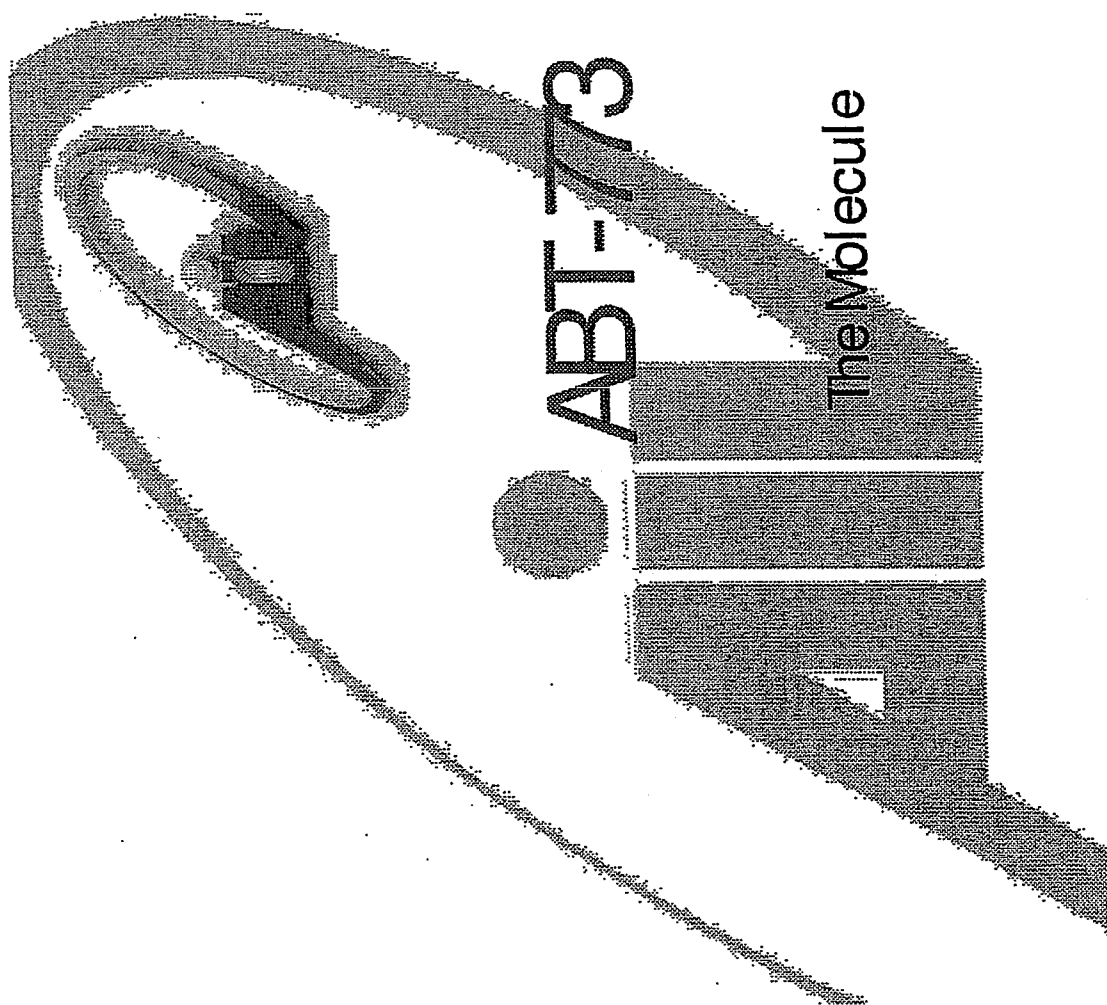
+++ Major Factor

ABBT205051

Confidential



ABBT205052



Confidential

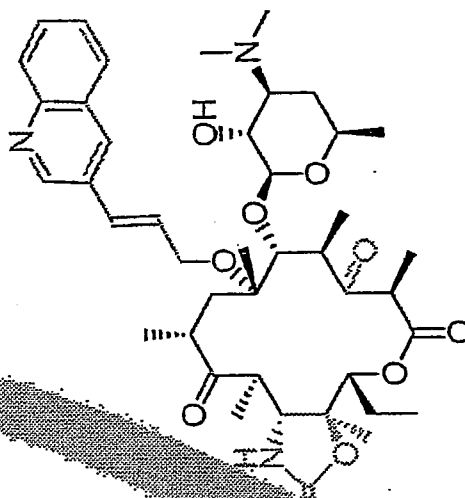
ABBT205053

## ABT-773 Keloidide

•Quinolinyl allyl propenyl moiety at the 6-  
0 -position

•Keto group at the 3-position

•Carbamate group at the  
11, 12-position

**ABT-773**

Confidential

ABBT205054



## ABT-773 Ketolide

### • Ketolides are a Novel Class of Antimicrobial

- Active includes key respiratory tract infection pathogens including macrolide and penicillin resistant *S. pneumoniae* and *S. pyogenes*
- Bactericidal activity
- Prolonged post antibiotic effect
- Reduced resistance development

Confidential

ABBT205055

# Microbiology

Organism	MIC <sub>90</sub> µg/ml			
	ABT-773	Kelek	Clari	Azi
<i>S. pneumoniae</i> ery-S	0.008	0.004	0.03	0.12
<i>S. pneumoniae</i> mcl	0.12	1.0	4.0	16.0
<i>S. pneumoniae</i> erm	0.01	0.12	>32	>32
<i>S. pyogenes</i> ery-S	0.12	2.0	1.0	2.0
<i>S. pyogenes</i> ery-R	0.5	>8.0	>32	>32
<i>M. catarrhalis</i>	0.25	0.25	0.5	0.25
<i>H. Influenzae</i>	2.0	2.0	16	2.0
<i>Legionella</i>	2.0	2.0	0.06	1.0
<i>M. Pneumoniae</i>	<0.005	<0.005	0.008	<0.005
<i>C. Pneumoniae</i>	0.015	0.06	0.06	0.12

Confidential



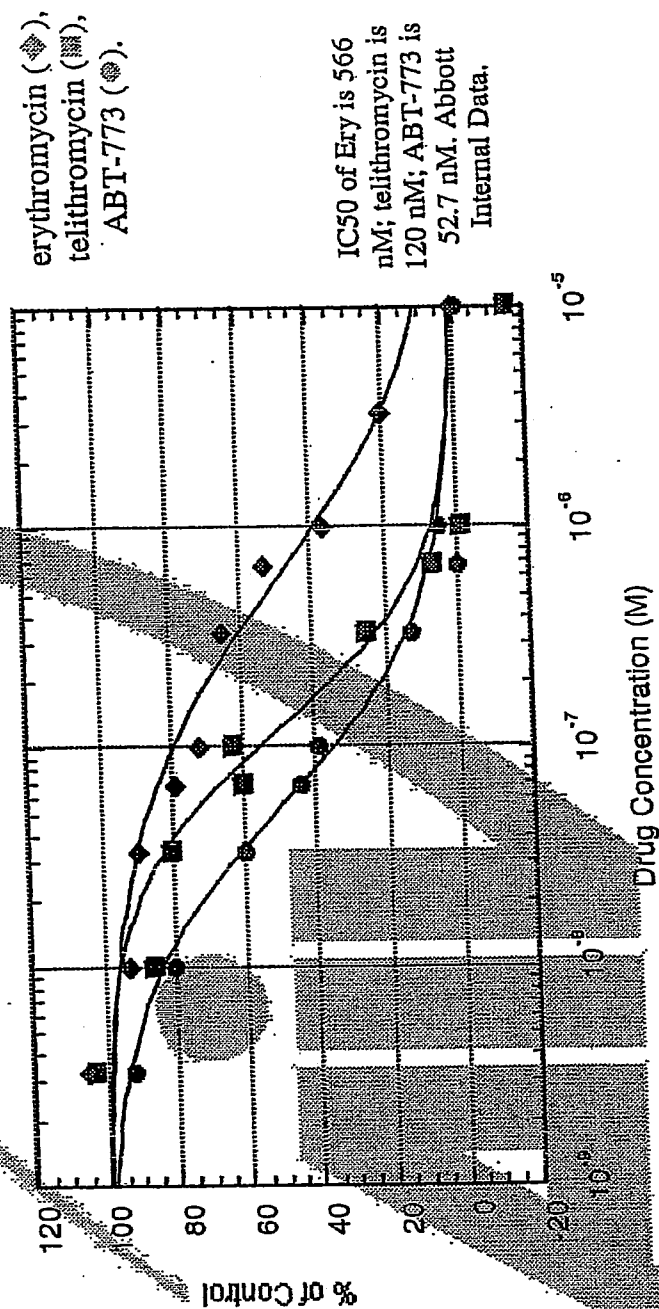


Confidential

ABBT205056

ABBT205057

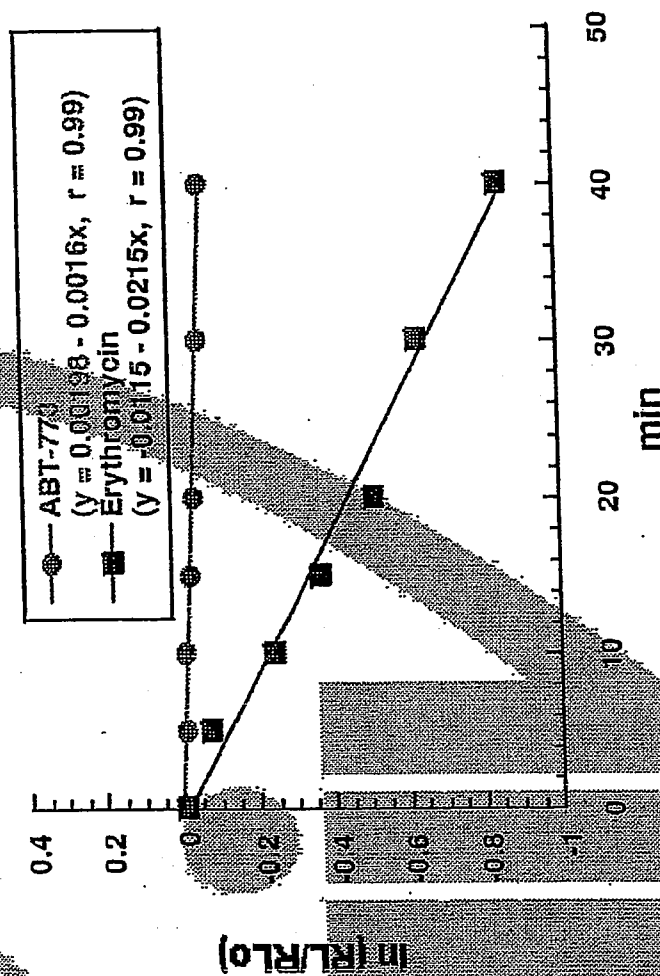
# Ribosome Binding, Susceptible *S. pneumoniae*



Confidential



# ABT-773 Displacement in Susceptible *S. pneumoniae* 2486

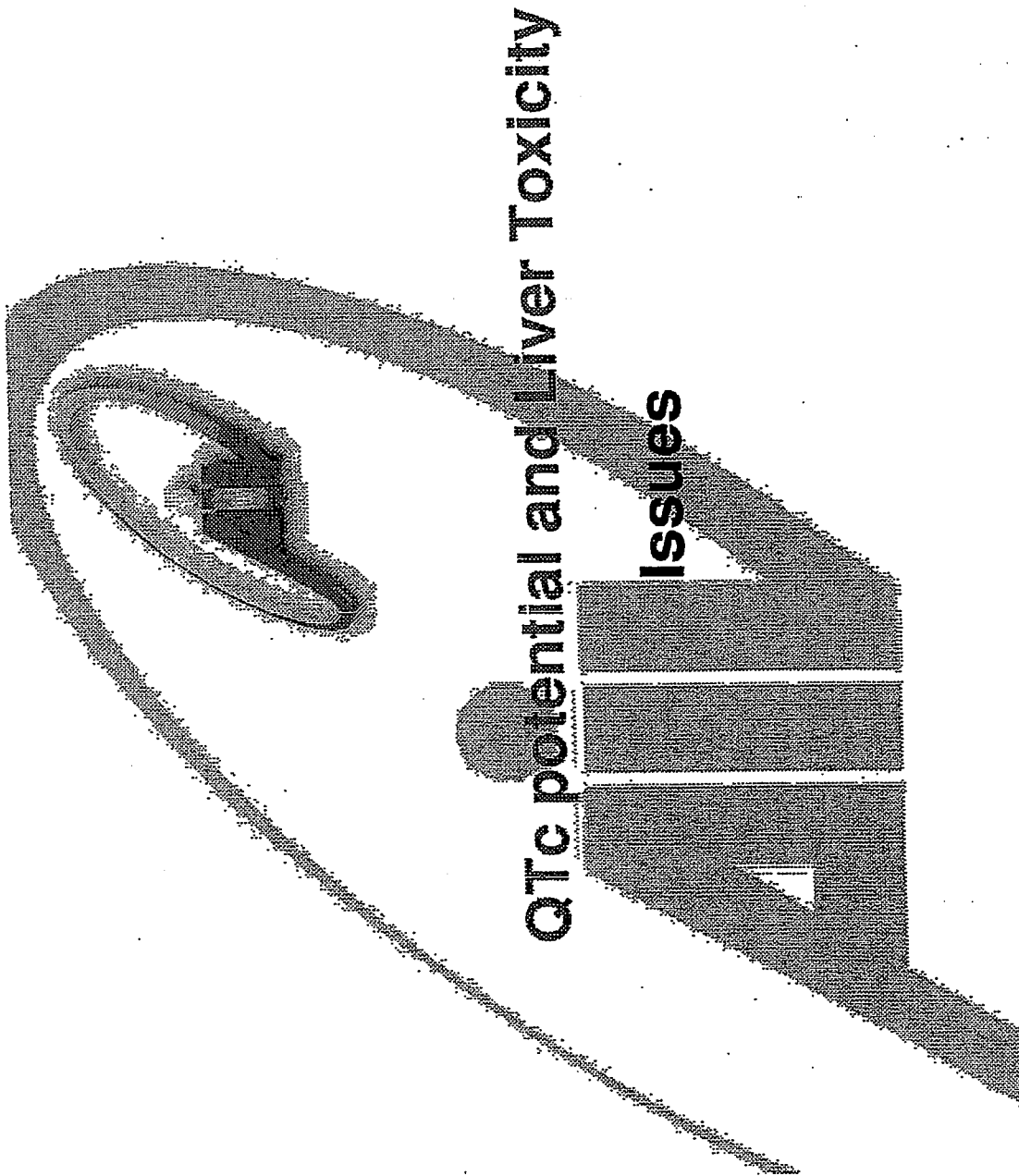


J. Capobianco et al.  
ICAAC 1999, #2137

ABBT205058

Confidential

ABBT205059



Confidential



ABBT205060

## QTc Prolongation Issues

- Potential for QTc Prolongation is a hot button worldwide
  - Antimicrobial agents including macrolides and quinolones are of concern to regulatory agencies
  - CPMP guidelines require data from animal models and 200 subjects
  - FDA is in the process of evaluating all drug class known to have a potential for prolonging QTc (erythromycin and clarithromycin)
  - FDA has question whether ketolides behave like macrolides
  - FDA requested additional dog tox work to evaluate QTc
  - Required to include ECG monitoring in pivotal Phase 3 studies
  - FDA may require a Phase I study in patients with underlying cardiac disease
  - Some antimicrobials now contain warnings for QT prolongation
  - Telithromycin (Ketek) data residing at FDA
    - Advisory Meeting rescheduled to May 2001 probably not related to QTc concerns

Confidential

ABBT205061

## QT<sub>c</sub> Prolongation Issues ABT-773

- Pre-clinical data positive for QTc dose response.
- A possible dose effect in Phase I at total daily dose  $\geq 800$  mg.
- No significant QT effect observed when ABT-773 was administered with the metabolic inhibitor ketoconazole. (Increased ABT-773 C<sub>max</sub> 5X)
- No concentration response in Phase I studies ( $\leq 300$ mg).
- No consistent QT effect observed at clinical doses studied in Phase II studies. (150 mg QD to 600 mg QD)

Confidential

ABBT205062

## QTc Prolongation Issues ABT-773 Plan

- Completed pre-clinical evaluation of ABT-773
- Completed ECG monitoring of >200 patients in Phase II and III
- Continue to monitor QTc and electrolytes in Phase III programs.
- Planning FDA requested study of QTc in patients with pre-existing cardiac disease.
- IV ABT-773 Phase I study will monitor QTc carefully
- Consult with Drs. Morganroth and Moss QTc advisors.

Confidential

ABBT205063

## Liver Toxicity Issues

- Potential for liver toxicity is a concern for the FDA
  - Recent liver toxicity seen with Trovofloxacin are of concern to regulatory agencies.
  - Gemifloxacin recently not approved by FDA because of liver toxicity concerns.
  - FDA meeting on guides to industry on how to study liver function scheduled for February 11-12, 2001

Confidential

ABBT205064

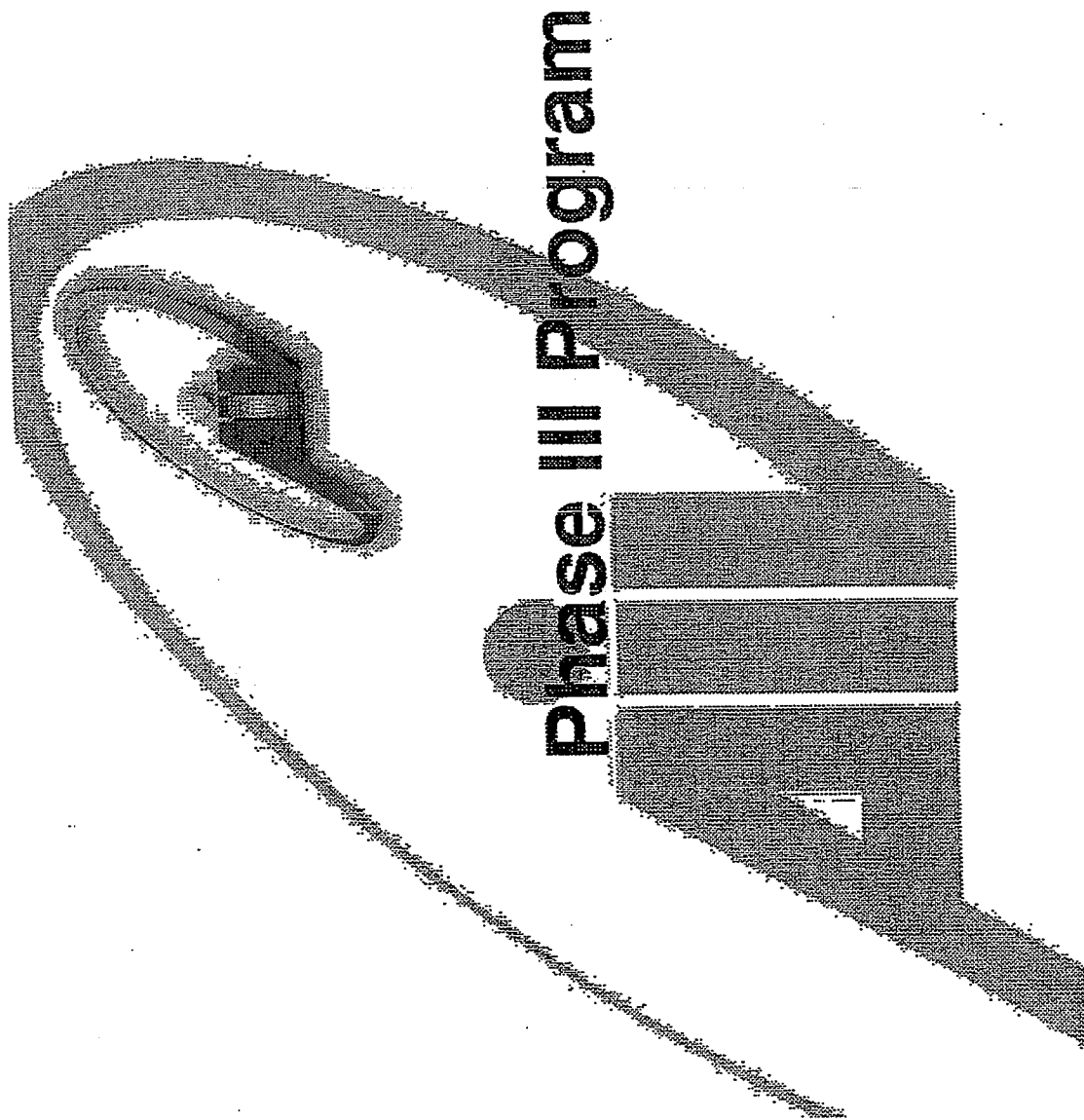
## **Liver Toxicity Issues for ABBT-773**

- Preclinical tox showed some effect on the liver function.
- Japanese in bridging study showed increased LFTs.
- No evidence of LFT issue in Western subjects.
- No evidence of dose response.
- Repeat of Japanese bridging study in Japan showed No evidence of LFT increases in Japanese or Caucasians.
- ABBT-773 plan for accessing problem
  - Continue to monitor LFT in Phase III programs.
  - Jean Fox will attend FDA meeting.

Confidential



ABBT205065



Confidential

ABBT205066

## Phase III Program Proposed Indications and Treatment Duration

Infection	Dosage	Duration
Pharyngitis/Tonsillitis due to: <i>S. pyogenes</i> *	150 mg QD	5 d
Acute bacterial sinusitis due to:		
<i>H. influenzae</i>	150 mg QD or BID	10 d
<i>M. catarrhalis</i>	150 mg QD or BID	10 d
<i>S. pneumoniae</i> **	150 mg QD or BID	10 d
Acute bacterial exacerbation of chronic bronchitis due to:		
<i>H. influenzae</i>	150 mg	5 d
<i>H. parainfluenzae</i>	150 mg	5 d
<i>M. catarrhalis</i>	150 mg	5 d
<i>S. pneumoniae</i> **	150 mg	5 d
Community-acquired pneumonia due to:		
<i>S. pneumoniae</i>	150 mg QD or BID	10 d
<i>H. influenzae</i>	150 mg QD or BID	10 d
<i>L. pneumophila</i>	150 mg QD or BID	10 d
<i>M. pneumoniae</i>	150 mg QD or BID	10 d
<i>S. pneumoniae</i> **	150 mg QD or BID	10 d

\*including macrolide-resistant strains.  
\*\*including penicillin-resistant and macrolide-resistant strains.

Confidential

ABBT205067

**Phase III Program  
Studies Started in Year 2000**

Study	Indication	ABT-773 Regimen	Comparator	Number Subjects	Location
M00-223	Pharyngitis	150 mg QD 5 days	Penicillin V	185/520	US (IND)
M00-222	Pharyngitis	150 mg QD 5 days	Penicillin V	0/520	EU (Non-IND)
M00-216	ABEOB	150 mg QD 5 days	Azithromycin	131/600	US, Canada IND
M00-217	ABEOB	150 mg QD 5 days	Levofloxacin	0/500	EU (Non-IND)

Confidential



ABBT205068

**Phase III Program  
Studies Started in Year 2000, Con't**

**Dose Finding Studies for Sinusitis/CAP:**

Study	Indication	ABT-773 Regimen	Comparator	Number Subjects	Location
M00-225	Sinusitis	150 mg QD vs. 150 mg BID 10 days	None	137/500	US, EU (IND)
M00-219	CAP	150 mg QD vs. 150 mg BID 10 days	None	76/500	US, Canada, EU (IND)

Confidential

ABBT205069

## Dosing Issue

### 150 mg BID vs 150 mg QD: Background

- Phase II data indicated 300 mg QD was not viable due to high levels of diarrhea (10-20%) and taste perversion (10-20%)
- Phase II ABECB and pharyngitis/tonsillitis data supported 150 mg QD
  - 150 mg QD currently being evaluated in ongoing phase III trials in these indications
- Dosing selection for CAP and sinusitis confounded by limited data
  - few bacterial isolates, particularly with H. flu in sinusitis
  - no 150 mg arm in CAP trial
- To increase probability of correct dose selection in CAP/sinusitis, the decision was made to undertake additional studies to generate more data in these indications
  - 150 mg QD vs 150 mg BID CAP & sinusitis trials ongoing
  - Decision facilitated by Decision Support Group, with joint AI & PPD consensus on decision

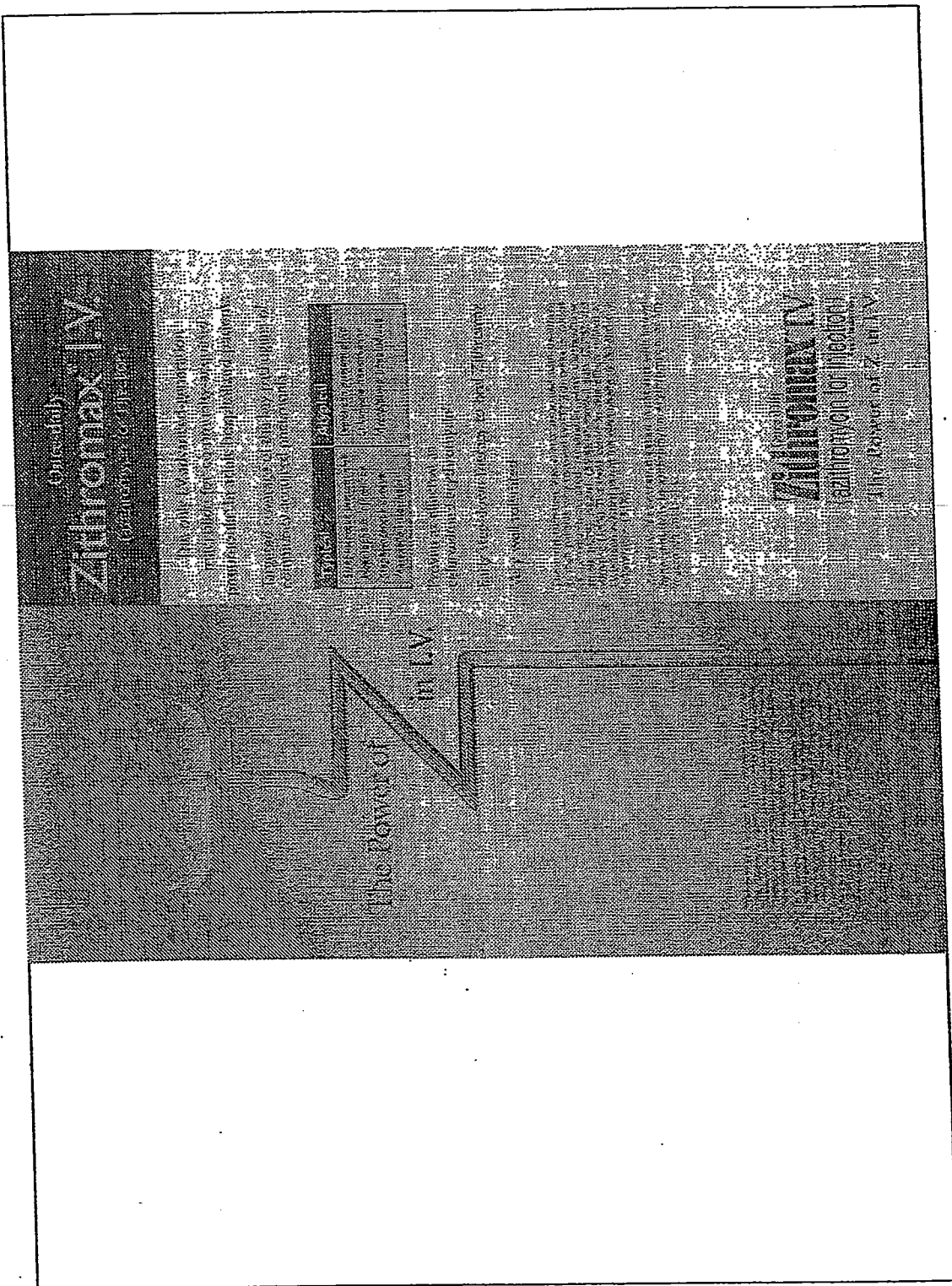
Confidential

ABBT205071



Confidential





**Orally**  
**Zithromax® IV.**  
Ceftriaxone for Injection

It's the standard of care for the treatment of community-acquired pneumonia (CAP) and other serious infections. Zithromax IV is the only intravenous formulation of ceftriaxone available in the United States. It's the power of Z in IV.

**Key Features:**

- Single-dose therapy
- No need for renal adjustment
- No need for IV fluids
- No need for IV piggyback

**Indications:**

- Community-acquired pneumonia (CAP)
- Hospital-acquired pneumonia (HAP)
- Nosocomial pneumonia (NP)
- Bacteremia
- Meningitis
- Gonorrhea
- Syphilis
- Lyme disease
- Anthrax
- Botulism
- Tetanus
- Diphtheria
- Pertussis
- Whooping cough
- Measles
- Rubella
- Mumps
- Varicella
- Herpes
- HIV
- AIDS
- Kaposi's sarcoma
- Lymphoma
- Leukemia
- Myeloma
- Multiple myeloma
- Osteosarcoma
- Ewing's sarcoma
- Neuroblastoma
- Rhabdomyosarcoma
- Wilms' tumor
- Hepatocellular carcinoma
- Adenocarcinoma
- Squamous cell carcinoma
- Basal cell carcinoma
- Melanoma
- Glioma
- Astrocytoma
- Oligodendroglioma
- Ependymoma
- Medulloblastoma
- Neuroblastoma
- Rhabdomyosarcoma
- Wilms' tumor
- Hepatocellular carcinoma
- Adenocarcinoma
- Squamous cell carcinoma
- Basal cell carcinoma
- Melanoma
- Glioma
- Astrocytoma
- Oligodendroglioma
- Ependymoma
- Medulloblastoma

**The Power of Z**

**Z**

**IV**

**Zithromax IV**  
ceftriaxone for injection  
The Power of Z in IV

ABBT205073

## ABT-773 IV Formulation Strategic, Commercial, and Technical Value

### Strategic Value

- IV represents a channel not currently served by Anti-infective Franchise
- Leverages presence of Medical Center Reps and experience with ID community

### Commercial Value

- IV availability figures favorably into decisions regarding formulary access to molecule
  - potential advantage over tellthromycin, which will not have an IV
  - required to compete effectively with Zithromax, Tegulin, Avelex which have IVs
- Positive impact on tablet formulation
  - estimated \$36MM incremental to peak tablet sales due to step-down therapy
  - Enhances overall "potency" image of brand

### Technical Value

- Support for *S. pneumoniae* Resistance claim
  - FDA indicated that bacteremic patients will be important to establish body of evidence for this claim
- Provides additional information on QT effects

IV launch currently lags tablet launch by 1 year; any further delays will reduce the potential value

Confidential

ABBT205074

## ABT-773 IV Program Formulation Objectives

- Reconstituted solution . Once a day dosing. Low pain on injection
- Lyophilized powder, consisting of ABT-773 and a counter ion base.
- One strength, in a flip-top vial and the ADD Vantage system at launch.
- Diluent volume 100ML, with length of infusion (30 to 60 minutes) and type of diluent (Dextrose 5% and/or normal saline) TBD based on animal pain models, clinical and stability studies.

Confidential



ABBT205075

## ABT-773 IV Formulation PPD/HPD Funding Status

- PPD/HPD Collaboration initiated 9/99
- PPD funded Program 01/00-08/00 (\$1.4MM)
  - Formulation development ( lactate salt, lyophilized powder)
  - Animal pain models
  - Two week Tox study (monkey)
- HPD funded Program 08/00-12/00 (\$0.8MM)
  - Two week Tox study (rat)
  - Clinical supplies for Phase I
  - Stability program
- 2001 funding
  - HPD first pass funding cut for 773 IV (\$7MM)
  - Milestone funding to Phase I Go/No Go (\$1MM)
- Total program development costs 2000 - 2003 (\$22.5MM)

Confidential

ABBT205076

## **ABT-773 IV Formulation Animal Pain Study Results**

- Assessed 6 prototypes (3 different counter ions at 2 pH levels) vs clarithromycin IV and azithromycin IV
- Animal pain models showed no differentiation among all three compounds
  - Results not conclusive
  - Need to evaluate in humans
- Chose ABBT-773 lactate as the prototype to test in Phase I studies based on manufacturability and stability.

Confidential



ABBT205077

## ABT-773 IV Planned Clinical Program

*With 2001 funding decision in Feb:*

- Single Dose-rising Phase I study
- Multiple Dose Phase I with selected dose
- File US IND
- Initiate Phase III
  - 2 step-down CAP studies (US/Europe)
  - 2-3 days dosing
  - Two seasons to complete
- Filing

Apr/01  
June/01  
Oct/01  
Dec/01  
  
Aug/03

Confidential

ABBT205078

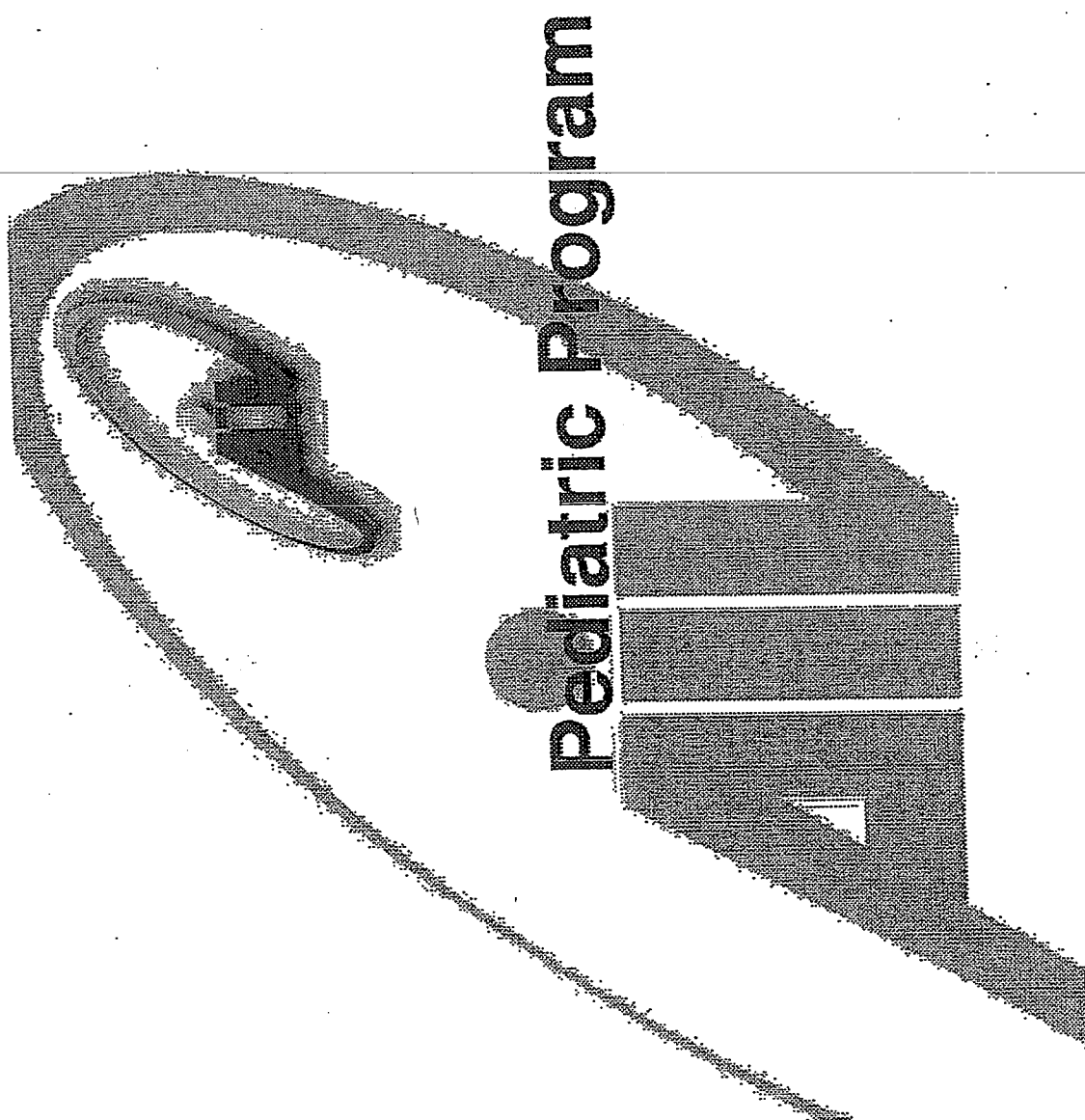
## ABT 773 IV Program Summary

### • Comments

- Funding for '01 not available PPD/HPD
- Go/No go could be made after Phase I based on safety profile (pain, QT, GI)
- Milestone funding recommended (\$1MM)
- Assuming Go, '01 budget estimated \$7MM
- IV will help to obtain resistant *S. pneumo* claim
- Total Program Cost 2000-2003 (\$22.5MM)

Confidential

ABBT205079



Confidential

ABBT205080

## **ABT-773 Pediatric Formulation Importance to the 773 program**

- Increased perception of safety
- Better pricing and acceptance in European markets
- FDA requires studies in pediatrics

Confidential

## ABT-773 Pediatric Program Formulation Objectives

- Develop coated particle formulae for global use
  - coated particles for Suspension - 150mg/5mL & 300mg/5mL
  - coated particles as a dry syrup, sprinkle or sachet.
- Desired Properties
  - Once a Day Dosing
  - Acceptable 'Initial Taste'
  - Minimal 'After Taste'
  - No Unpleasant Mouth-feel
  - Acceptable Color and Flavor
  - No Refrigeration Required.

Confidential

ABBT205081



ABBT205082

## ABT-773 Pediatric Program Taste Assessment

### Sensory Analysis of Uncoated Drugs Summary of Results

The three drug substances can be ranked from most to least bitter as follows:

Drug Substance	Concentration (ppm) Which Exhibits an Initial Bitter Intensity $\leq 1$ (Slight)
ABT-773	0.79
Clarithromycin	4.2
Azithromycin	15

- ABT-773 is approximately five times more bitter than clarithromycin

Confidential

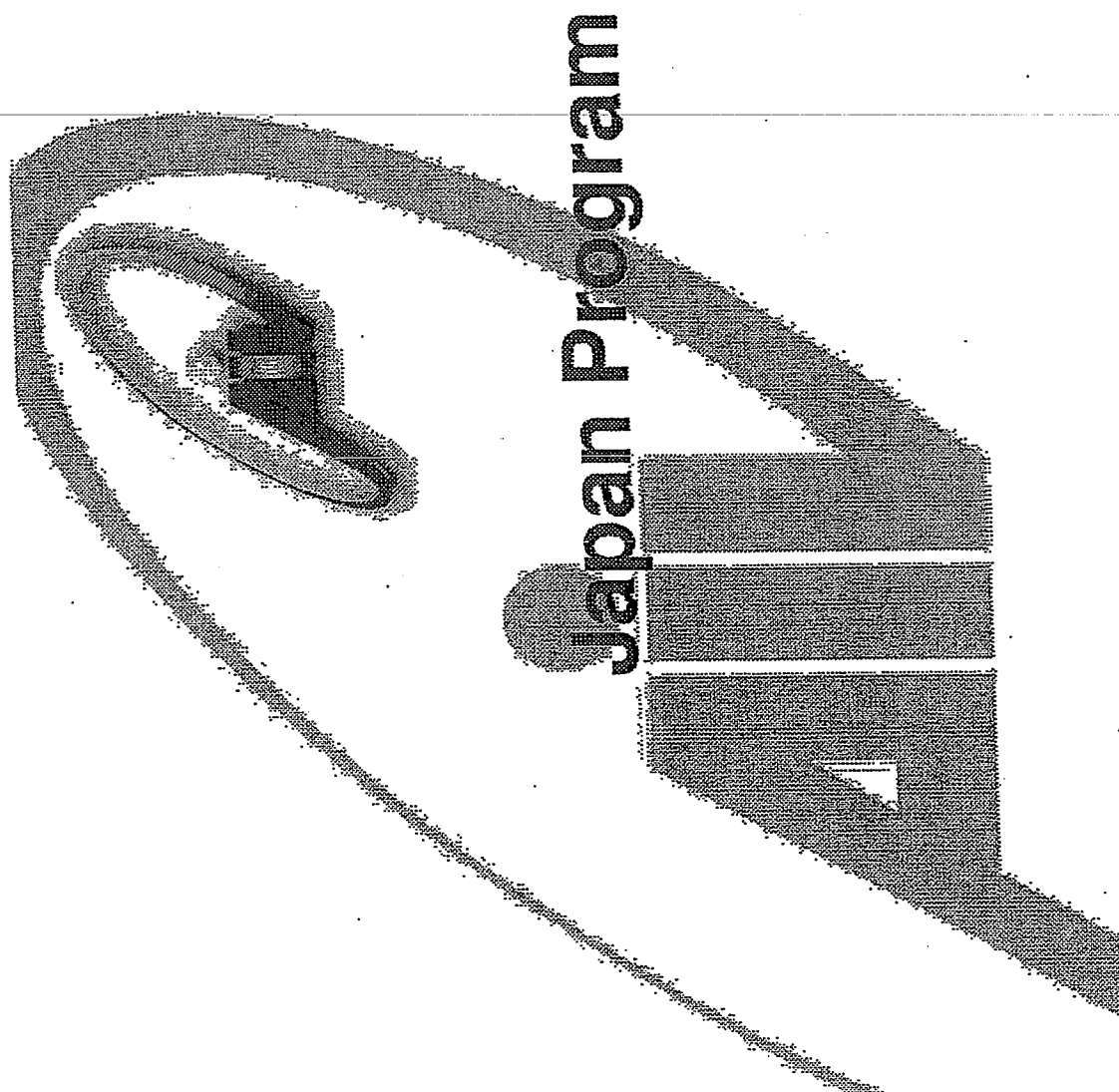
## ABT-773 Pediatric Program Taste Assessment

- The ABT-773 encapsulated prototype #2 may be at risk of dosing compliance problems due to flavor quality.
- Overall ABT-773 Prototype 2
  - Less bitter than Biaxin both initial and after taste
  - More bitter than Zithromax both initial and after taste
- For ABT-773 Prototype 2, the flavoring aromatics and sweetness decay quickly, exposing the bitterness which lingers throughout the aftertaste at or above the "concern" intensity level.

Confidential

ABBT205083

ABBT205084



Confidential



ABBT205085

## Japan Program Taisho

- Japan development is planned in coordination with Taisho and Dainabot
- Meetings are held at least 3 times a year to review developments
- Taisho funds 10.69% of global development costs and 50% of local Japan costs
- Bridging strategy is primary plan for development in Japan

Confidential

ABBT205086

## Japan Program Clinical Plan

• Phase I in Japan	<u>Start</u>
– Food Effect Study	Completed
– Single and multiple dose study	Completed
– Review data (Abbott/Taisho)	April/01
• PK data Japanese vs Caucasian	
• Development program strategy	
– Present Kiko data and recommend development program	
May/01	
– Start Tissue Conc. Study	2Q/01

Confidential

ABBT205087

## Japan Program Clinical Plan

- PK similar in Japanese and Caucasians (12/02 filing)
  - Recommend to Kiko same dose in Japan as in ex-Japan
  - Recommend to Kiko one comparative bridging study in CAP (Phase III) and several smaller local studies in skin infections, dentistry, otolaryngology, UTI and pan-bronchiolitis
  - Taisho agreement necessary prior to Kiko meeting
- PK different in Japanese and Caucasians (12/03 filing)
  - Phase II dose ranging study in CAP (Bridging study)
  - Phase III comparative study will be required
  - Full development time line
  - Implications on Taisho cost-sharing

Confidential

**PLs' IQ**



Jeanne M  
Fox/LAKE/PPRD/ABBOTT  
02/14/2001 01:04 PM

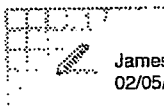
To James Steck/LAKE/PPRD/ABBOTT@ABBOTT  
cc Lawrence E Roebel/LAKE/PPRD/ABBOTT@ABBOTT

bcc

Subject Re: Studies to Meet Pediatric Rule Requirements

I share your concern and have an even bigger one. In those cases where we are planning to develop an NCE, and we have a target NDA date, I have had difficulty convincing people they have to take the pediatric rule requirements seriously. The answer I keep getting on ABT-773 is "but that project isn't funded". I don't think FDA will buy that answer.

James Steck



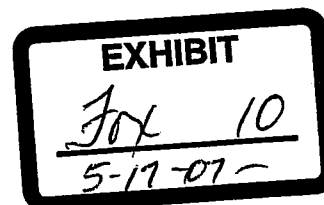
James Steck  
02/05/2001 05:20 PM

To: Jeanne M Fox/LAKE/PPRD/ABBOTT@ABBOTT, Lawrence E Roebel/LAKE/PPRD/ABBOTT@ABBOTT  
cc:  
Subject: Studies to Meet Pediatric Rule Requirements

Jeanne and Mick

This is just a heads up to let you know that there may be some issues arising in the future about concerns for being able to do studies requested by FDA to meet pediatric rule requirements because these studies "are not funded". Steve and I are running into discussions on this for Depakote ER in migraine where FDA has asked us to do an efficacy study in migraine per the pediatric rule. Of course we will attempt to negotiate with FDA to do the least onerous studies that will still satisfy the pediatric rule requirements, but folks will need to be advised at some point (preferably early on) that meeting this rule is a regulatory obligation and a cost of doing business. I'd appreciate hearing any thoughts you have on this subject.

Jim



CONFIDENTIAL  
ABBT0568172

**PLs' IW**



Marleen H  
Verlinden /LAKE/PPRD/ABB  
OTT

03/31/2001 09:50 PM

To Eugene X Sun/LAKE/PPRD/ABBOTT@ABBOTT

cc Carl Craft/LAKE/PPRD/ABBOTT@ABBOTT, Stan  
Bukotzer/LAKE/ABBOTT@ABBOTT, Richard G  
Granneman/LAKE/PPRD/ABBOTT@ABBOTT, John M  
Leonard/LAKE/PPRD/ABBOTT@ABBOTT

bcc

Subject Re: ABT-773

For what they are worth, here are my summary thoughts on the way forward with-773, QT issue:

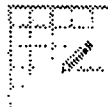
- despite significant issues with the quality of the QT data collection to date, a QT signal has emerged from both the pre-clinical and clinical programs.
- The numbers of patients with ECG data suffices to establish that there probably is an issue (i.e. N=200= criteria for exposing enough patients, in order not to miss a signal as laid out in CPMP guidelines ) have been met as hundreds of patients have had ECG data and a signal was indeed found
- the remaining question to be solved then is : what is the size of the QT effect ? and what is the size not only in healthy volunteers but also in patients at risk (defined in guidelines). The quantification entails a dedicated, super -defined experimental design (see QT project), with PBO , the therapeutic dose, a 3-5 times higher dose (600 mg, and potentially an arm with normal dose in presence of ketoconazole. Serial ECGs to be taken and rigorous timing of ECGs with detailed dose-response directed pK-pD analysis, XO design with subjects being own control. Because of the quality issue with QT data collected to date, the size of the QT effect might actually be larger than would appear from the current data.

For the populations at risk I would recommend considering that such patients be included in Phase III pivots and that in these subgroups, very standardized QT collection and reading be undertaken (as if it were a Phase I trial)

Hope this helps

Marleen

Eugene X Sun



Eugene X Sun  
03/30/2001 04:36 PM

To: Carl Craft/LAKE/PPRD/ABBOTT@ABBOTT, Joaquin M Valdes/LAKE/PPRD/ABBOTT@ABBOTT, Maria M Paris/LAKE/PPRD/ABBOTT@ABBOTT, Marleen H Verlinden/LAKE/PPRD/ABBOTT@ABBOTT, Perry D Nisen/LAKE/PPRD/ABBOTT@ABBOTT, Eltraim Shek/LAKE/PPRD/ABBOTT@ABBOTT, Reid Patterson/LAKE/PPRD/ABBOTT@ABBOTT, Xavier Frapaise/LAKE/ABBOTT@ABBOTT, Jeanne M Fox/LAKE/PPRD/ABBOTT@ABBOTT, Jennifer J Moore/LAKE/ABBOTT@ABBOTT, Nigel Livesey/LAKE/ABBOTT@ABBOTT, David D Morris/LAKE/PPRD/ABBOTT@ABBOTT, Margaret A Foley/LAKE/PPRD/ABBOTT@ABBOTT, Carol Olson/LAKE/PPD/ABBOTT@ABBOTT, Helen B Eliopoulos/LAKE/PPRD/ABBOTT@ABBOTT, Dawn M Carlson/LAKE/PPRD/ABBOTT@ABBOTT, Linda E Gustavson/LAKE/PPRD/ABBOTT@ABBOTT, Walid Awni/LAKE/PPRD/ABBOTT@ABBOTT, Bryan F Cox/LAKE/PPRD/ABBOTT@ABBOTT, Gary A Gintant/LAKE/PPRD/ABBOTT@ABBOTT, Jie X Zhang/LAKE/PPRD/ABBOTT@ABBOTT, Thao T Doan/LAKE/PPRD/ABBOTT@ABBOTT, Stan Bukotzer/LAKE/ABBOTT@ABBOTT, Richard G Granneman/LAKE/PPRD/ABBOTT@ABBOTT, Carol S Meyer/LAKE/PPRD/ABBOTT@ABBOTT

cc: John M Leonard/LAKE/PPRD/ABBOTT@ABBOTT

Subject: ABT-773

EXHIBIT

*Meyer 17*  
*5-22-07*

CONFIDENTIAL  
ABBT0571202

Summary and followup items from this morning's discussion on the potential for QT prolongation by ABT-773:

1. Europe:

The accumulated phase I/II data, as well as expected phase III data, will be assessed in the context of the CPMP guidance to determine to what extent the guidance has been met, and what additional clinical studies or clinical data, if any, are needed. This will be a joint effort of venture, AI regulatory, PK, and statistics.

2. FDA:

Although the FDA has expressed interest in seeing data from patients with cardiac compromise, it is not clear how this study would be conducted. It was mentioned that such studies were requested of Sepracor for norastemizole. It would be instructive to get further information on this if available. The Ketek advisory scheduled for 4/26 should provide some indication of the direction FDA will take with this class of drugs on this particular issue. The relevant groups will reconvene following this advisory.

3. Several outside experts in the field and with potential US and European regulatory insights will be contacted in the next several weeks. A package of data should be prepared and made available to them in advance, necessary CDA's prepared, and a block of time allocated to specifically discuss ABT-773. These advisors (and Abbott contacts) are Shah (Bryan), Malik (Marleen), Moss and Morganroth (venture). Meetings with these individuals should be coordinated such that the appropriate scientific, medical, and regulatory personnel are in attendance.

Thank you to those who prepared presentations this morning



**PLs' KP**



sblewitt@jhancock.co  
m

03/07/2000 03:29 PM

To: steve.cohen@abbott.com@INTERNET,  
phil.deemer@abbott.com@INTERNET  
Subject: Research and Development Transaction

This message is in MIME format. Since your mail reader does not understand this format, some or all of this message may not be legible.

Phil and Steve:

I am attaching a revised Summary of Terms for the Research and Development transaction that we have been discussing. The structure that we propose is highly dependent upon the number of compounds included in the transaction, the stage of development, and the expected sales, and must be considered only representative of a transaction that we might agree upon. For the sake of discussion, I have assumed six phase II compounds which are independent of each other (in terms of likelihood of receiving regulatory approval) and a basket of pre-clinical or phase I cancer compounds. I have further assumed that any, and all, compounds that receive regulatory approval will have maximum sales of \$600 million. We believe that a diversified basket of compounds should yield the investor an IRR of 20-25%. Based on your desire to reduce the cost of capital and our desire to lower our risk, we have built in milestone payments, a tiered royalty structure, and a termination date for the royalties. The model provides us with an expected yield of 18-22%.

<<abbott.doc>>

Steve.

CONFIDENTIAL  
AL 000132

**Proposed Summary of Terms**

3/7/00

**Researcher:** Abbott Laboratories ("Abbott")

**Funding Source:** John Hancock Life Insurance Company ("John Hancock")

**Use of Proceeds:** Fund research and development programs associated with Program Compounds.

**Program Compounds:** A minimum of six independent phase II (or later stage) compounds that have been mutually agreed upon, and selected earlier-stage cancer compounds, and any line extensions, new formulations and combination products in which the same active ingredient is present.

**Program Payments:** During the Program Term, and in consideration of Abbott's continuing performance of the research services under the Research Plan, John Hancock shall make program payments to Abbott in the installments and on the dates set forth below:

<u>Date</u>	<u>Payment</u>
[May 1,] 2000	\$50,000,000
[May 1,] 2001	\$50,000,000
[May 1,] 2002	\$50,000,000
[May 1,] 2003	\$50,000,000

"Program Term" means the period commencing [May 1,] 2000 Date and ending on [April 30,] 2003.

"Research Plan" means a detailed statement of Abbott's objectives, activities, timetable, FTE allocation and budget for the Program Compounds during the Program Term.

During the Program Term, Abbott agrees to spend a minimum of \$100 million per year on research and development programs associated with the Program Compounds

If Abbott ceases research and development of all Program Compounds or Abbott does not spend at least [\$] million in a year on the research and development of Program Compounds, John Hancock's obligation to continue to make Program Payments shall cease.

**CONFIDENTIAL**  
**AL 000133**

**Milestone**

**Payments:**

Abbott shall make a milestone payment in the amount of [\$10 million] for each Compound that receives Regulatory Approval. Payment will be made at the time of Regulatory Approval.

**Royalty**

**Payments:**

Abbott shall pay to John Hancock royalties on Net Sales of Program Compounds at the following rates:

<u>Annual Sales Volume</u>	<u>Royalty Rate</u>
0 to [\$400] million	[10%]
> [\$ 400] million and ≤ [\$1,000] million	[ 5%]
> [\$1,000] million	[ 2%]

The obligation to make royalty payments shall commence on the date of the First Commercial Sale of a Program Compound [in a given country] and shall continue with respect to Net Sales of such Program Compound [sold in such country] for a period of [10] years.

**Development, Manufacturing,  
And Marketing Agreements:**

Abbott shall be solely responsible for, and agrees to use reasonable commercial efforts to pursue, the clinical development, government approval, manufacturing, marketing and sales of the Program Compounds.

PLS' KQ

Abbott

Page 1 of 1

---

**From:** Stephen Blewitt [stephenblewitt@mediaone.net]  
**Sent:** Sunday, April 02, 2000 10:24 PM  
**To:** Blewitt, Stephen  
**Subject:** Abbott

Steve,

Steve.

CONFIDENTIAL  
JH 001707

[illegible]

1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
2	0	0	0	0	0	0	0	0	0	0	1	0	0	35	91	210	350	560	630	700	700	700	595	525	455	350
3	1	1	1	1	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2230	1945	1695	1355	
4	1	1	1	1	0	0	0	0	0	0	4	0	0	90	269	631	1130	1842	2300	2630	2820	2630	2345	2095	1695	
5	0	1	0	0	0	0	0	0	0	0	1	0	0	60	156	360	600	960	1080	1200	1200	1020	900	780	600	
6	1	1	0	1	1	0	0	0	0	0	4	0	0	95	282	661	1180	1922	2390	2730	2920	2960	2715	2420	2160	1745
7	0	0	1	1	1	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1105	975	845	650	
8	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
9	1	1	0	1	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
10	0	1	0	1	0	0	0	0	0	0	2	0	0	95	247	570	950	1520	1710	1900	1900	1900	1615	1425	1235	950
11	0	0	0	1	0	0	0	0	0	0	1	0	0	35	91	210	350	560	630	700	700	595	525	455	350	
12	1	0	1	1	0	0	0	0	0	0	2	0	0	30	113	271	510	830	1100	1230	1300	1210	1045	915	755	
13	0	1	1	1	1	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
14	1	1	0	1	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
15	0	0	1	0	0	0	0	0	0	0	1	0	0	30	78	180	300	480	540	600	600	600	510	450	390	300
16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	1	0	0	0	1	0	0	0	0	0	2	0	0	35	126	301	560	910	1190	1330	1400	1400	1295	1120	980	805
19	1	1	1	1	1	1	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
20	1	1	1	1	1	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
21	1	0	1	1	1	1	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
22	1	0	1	0	1	0	0	0	0	0	3	0	0	30	113	271	530	882	1220	1430	1620	1660	1610	1445	1315	1095
23	0	0	0	1	0	0	0	0	0	0	1	0	0	35	91	210	350	560	630	700	700	700	595	525	455	350
24	0	1	1	1	1	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
25	1	0	1	1	1	1	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
26	0	0	1	0	0	0	0	0	0	0	1	0	0	30	78	180	300	480	540	600	600	600	510	450	390	300
27	0	1	0	0	0	0	0	0	0	0	1	0	0	60	156	360	600	960	1080	1200	1200	1200	1020	900	780	600
28	1	1	1	1	1	1	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
29	0	1	1	1	1	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
30	0	0	1	1	1	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1105	975	845	650	
31	0	1	1	1	1	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
32	0	1	1	1	1	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
33	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	20	52	120	200	320	360	400	400	400	340
34	1	1	1	1	0	1	0	0	0	0	4	0	0	90	269	631	1130	1842	2300	2630	2820	2860	2630	2345	2095	1695
35	0	1	0	0	1	0	0	0	0	0	2	0	0	60	156	360	620	1012	1200	1400	1520	1560	1420	1300	1180	940
36	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
38	0	1	1	1	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250

**CONFIDENTIAL**  
**JH 001708**

Page 2

**CONFIDENTIAL**  
**JH 001709**



Sheet1

101	1	1	1	1	0	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
102	0	1	0	1	0	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
103	1	1	1	1	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2230	1945	1695	1355	
104	1	0	0	1	0	0	0	0	0	0	0	2	0	0	35	126	301	560	910	1190	1330	1400	1400	1295	1120	980	805
105	0	0	0	1	0	0	0	0	0	0	0	1	0	0	35	91	210	350	560	630	700	700	700	595	525	455	350
106	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
107	1	1	0	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
108	0	1	1	0	0	0	0	0	0	0	0	2	0	0	90	234	540	900	1440	1620	1800	1800	1800	1530	1350	1170	900
109	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
110	0	0	0	1	0	0	0	0	0	0	0	1	0	0	35	91	210	350	560	630	700	700	700	595	525	455	350
111	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
112	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
113	0	1	0	0	0	0	0	0	0	0	0	1	0	0	60	156	360	600	960	1080	1200	1200	1200	1020	900	780	600
114	0	1	0	0	1	0	0	0	0	0	0	2	0	0	60	156	360	620	1012	1200	1400	1520	1560	1420	1300	1180	940
115	0	1	1	1	1	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
116	1	0	1	1	1	1	0	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
117	0	1	1	1	1	1	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
118	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
119	0	1	1	1	0	0	0	0	0	0	0	2	0	0	90	234	540	900	1440	1620	1800	1800	1800	1530	1350	1170	900
120	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
121	0	1	0	0	1	0	0	0	0	0	0	2	0	0	60	156	360	620	1012	1200	1400	1520	1560	1420	1300	1180	940
122	1	1	1	1	0	1	0	0	0	0	0	4	0	0	90	269	631	1130	1842	2300	2630	2820	2860	2630	2345	2095	1695
123	1	0	1	1	0	0	0	0	0	0	0	2	0	0	30	113	271	510	830	1100	1230	1300	1300	1210	1045	915	755
124	1	1	1	1	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
125	1	0	0	1	0	0	0	0	0	0	0	2	0	0	35	126	301	560	910	1190	1330	1400	1400	1295	1120	980	805
126	1	1	0	0	0	0	0	0	0	0	0	2	0	0	60	191	451	810	1310	1640	1830	1900	1900	1720	1495	1305	1055
127	1	1	1	1	0	1	0	0	0	0	0	4	0	0	90	269	631	1130	1842	2300	2630	2820	2860	2630	2345	2095	1695
128	1	1	1	1	1	1	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
129	0	1	1	0	1	0	0	0	0	0	0	3	0	0	90	234	540	920	1492	1740	2000	2120	2160	1930	1750	1570	1240
130	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
131	1	0	1	0	0	0	0	0	0	0	0	2	0	0	30	113	271	510	830	1100	1230	1300	1300	1210	1045	915	755
132	1	1	0	0	0	0	0	0	0	0	0	2	0	0	60	191	451	810	1310	1640	1830	1900	1900	1720	1495	1305	1055
133	0	1	1	1	1	1	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
134	1	0	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
135	1	0	0	1	1	0	0	0	0	0	0	3	0	0	35	126	301	580	962	1310	1530	1720	1760	1695	1520	1380	1145
136	1	0	1	1	1	1	0	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
137	0	0	1	0	0	0	0	0	0	0	0	1	0	0	30	78	180	300	480	540	600	600	600	510	450	390	300
138	1	1	1	1	0	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
139	1	1	1	1	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
140	0	1	1	1	1	1	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
141	0	0	1	1	1	0	0	0	0	0	0	3	0	0	65	169	390	670	1092	1290	1500	1620	1660	1505	1375	1245	990
142	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
143	1	0	1	1	1	1	0	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
144	1	0	1	1	1	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
145	0	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
146	1	0	0	1	1	1	0	0	0	0	0	3	0	0	35	126	301	580	962	1310	1530	1720	1760	1695	1520	1380	1145
147	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
148	1	1	1	1	1	1	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
149	0	1	0	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
150	1	1	1	1	0	1	0	0	0	0	0	4	0	0	90	269	631	1130	1842	2300	2630	2820	2860	2630	2345	2095	1695
151	1	0	1	1	0	0	0	0	0	0	0	2	0	0	30	113	271	510	830	1100	1230	1300	1300	1210	1045	915	755
152	0	1	0	0	1	0	0	0	0	0	0	2	0	0	60	156	360	620	1012	1200	1400	1520	1560	1420	1300	1180	940
153	1	0	1	1	1	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
154	0	0	1	1	0	0	0	0	0	0	0	1	0	0	30	78	180	300	480	540	600	600	600	510	450	390	300
155	0	1	1	1	1	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
156	1	0	0	1	1	1	0	0	0	0	0	3	0	0	35	126	301	580	962	1310	1530	1720	1760	1695	1520	1380	1145
157	1	0	1	1	1	1	0	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
158	0	1	0	1	1	1	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
159	1	1	0	0	1	0	0	0	0	0	0	3	0	0	60	191	451	830	1362	1760	2030	2220	2260	2120	1895	1705	1395

Sheet1

[illegible]

**CONFIDENTIAL**  
**JH 001711**

Sheet1

225	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
226	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
227	0	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
228	1	1	1	1	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
229	0	0	1	1	1	0	0	0	0	0	0	3	0	0	65	169	390	670	1092	1290	1500	1620	1660	1505	1375	1245	990
230	1	0	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
231	0	1	0	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
232	0	1	0	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
233	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
234	1	1	1	1	0	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
235	0	1	1	0	1	0	0	0	0	0	0	3	0	0	90	234	540	920	1492	1740	2000	2120	2160	1930	1750	1570	1240
236	0	1	0	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
237	1	0	1	1	1	0	0	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
238	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
239	1	1	0	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
240	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
241	0	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
242	0	1	1	0	1	0	0	0	0	0	0	3	0	0	90	234	540	920	1492	1740	2000	2120	2160	1930	1750	1570	1240
243	0	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
244	0	0	0	1	1	0	0	0	0	0	0	2	0	0	35	91	210	370	612	750	900	1020	1060	995	925	855	690
245	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
246	1	0	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
247	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
248	1	0	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
249	1	0	1	1	1	0	0	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
250	1	0	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
251	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
252	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	35	91	210	350	560	630	700	700	700	595	525	455
253	0	1	0	1	0	0	0	0	0	0	0	2	0	0	95	247	570	950	1520	1710	1900	1900	1900	1615	1425	1235	950
254	0	1	0	0	1	0	0	0	0	0	0	2	0	0	60	156	360	620	1012	1200	1400	1520	1560	1420	1300	1180	940
255	0	1	1	0	1	0	0	0	0	0	0	3	0	0	90	234	540	920	1492	1740	2000	2120	2160	1930	1750	1570	1240
256	1	0	1	0	1	0	0	0	0	0	0	3	0	0	30	113	271	530	882	1220	1430	1620	1660	1610	1445	1315	1095
257	1	0	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
258	1	1	0	1	1	0	0	0	0	0	0	4	0	0	95	282	661	1180	1922	2390	2730	2920	2960	2715	2420	2160	1745
259	0	0	1	0	0	0	0	0	0	0	0	1	0	0	30	78	180	300	480	540	600	600	600	510	450	390	300
260	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
261	0	0	1	0	0	0	0	0	0	0	0	1	0	0	30	78	180	300	480	540	600	600	600	510	450	390	300
262	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
263	1	0	0	1	1	0	0	0	0	0	0	3	0	0	35	126	301	580	962	1310	1530	1720	1760	1695	1520	1380	1145
264	0	0	0	1	1	0	0	0	0	0	0	2	0	0	35	91	210	370	612	750	900	1020	1060	995	925	855	690
265	1	0	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
266	1	0	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
267	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
268	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
269	0	0	1	1	1	0	0	0	0	0	0	3	0	0	65	169	390	670	1092	1290	1500	1620	1660	1505	1375	1245	990
270	1	1	0	0	1	0	0	0	0	0	0	3	0	0	60	191	451	830	1362	1760	2030	2220	2260	2120	1895	1705	1395
271	0	0	1	0	0	0	0	0	0	0	0	1	0	0	30	78	180	300	480	540	600	600	600	510	450	390	300
272	0	1	1	0	1	0	0	0	0	0	0	3	0	0	90	234	540	920	1492	1740	2000	2120	2160	1930	1750	1570	1240
273	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
274	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
275	0	1	0	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
276	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
277	0	1	0	0	0	0	0	0	0	0	0	1	0	0	60	156	360	600	960	1080	1200	1200	1200	1020	900	780	600
278	1	1	1	1	0	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
279	1	1	0	1	1	0	0	0	0	0	0	4	0	0	95	282	661	1180	1922	2390	2730	2920	2960	2715	2420	2160	1745
280	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
281	1	0	1	0	0	0	0	0	0	0	0	2	0	0	30	113	271	510	830	1100	1230	1300	1300	1210	1045	915	755
282	0	0	1	1	0	0	0	0	0	0	0	3	0	0	65	169	390	670	1092	1290	1500	1620	1660	1505	1375	1245	990
283	0	0	0	1	0	0	0	0	0	0	0	1	0	0	35	91	210	350	560	630	700	700	700	595	525	455	350

Page 6

Sheet1

349	1	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
350	1	0	1	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
351	1	0	1	1	1	0	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
352	0	1	1	1	0	0	0	0	0	0	0	0	2	0	0	90	234	540	900	1440	1620	1800	1800	1800	1530	1350	1170	900
353	1	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
354	1	1	0	0	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
355	1	0	0	0	1	1	0	0	0	0	0	0	2	0	0	0	35	91	230	402	680	830	1020	1050	1100	995	925	795
356	0	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0	0	0	20	52	120	200	320	360	400	400	400	340
357	0	1	1	1	0	0	0	0	0	0	0	0	2	0	0	90	234	540	900	1440	1620	1800	1800	1800	1530	1350	1170	900
358	1	1	0	1	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
359	0	0	0	1	1	1	0	0	0	0	0	0	2	0	0	35	91	210	370	612	750	900	1020	1060	995	925	855	690
360	1	1	1	0	0	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
361	1	1	0	1	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
362	0	1	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
363	0	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
364	0	1	0	1	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
365	1	1	0	1	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
366	0	0	1	1	1	1	0	0	0	0	0	0	3	0	0	65	169	390	670	1092	1290	1500	1620	1660	1505	1375	1245	990
367	1	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
368	1	1	1	0	0	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
369	1	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
370	1	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
371	0	1	0	1	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
372	1	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
373	1	1	0	1	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
374	1	0	1	1	1	1	0	0	0	0	0	0	4	0	0	65	204	481	860	1442	1850	2130	2320	2360	2205	1970	1770	1445
375	1	0	1	1	1	1	0	0	0	0	0	0	4	0	0	65	204	481	860	1442	1850	2130	2320	2360	2205	1970	1770	1445
376	1	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
377	1	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
378	1	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
379	0	1	1	1	1	1	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
380	1	0	1	1	1	1	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
381	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
382	1	0	1	1	1	1	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
383	1	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
384	0	0	1	1	1	1	0	0	0	0	0	0	3	0	0	65	169	390	670	1092	1290	1500	1620	1660	1505	1375	1245	990
385	1	0	1	1	1	1	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
386	0	1	1	1	1	1	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250
387	1	1	0	0	0	0	0	0	0	0	0	0	2	0	0	60	191	451	810	1310	1640	1830	1900	1900	1720	1495	1305	1055
388	0	1	1	1	0	1	0	0	0	0	0	0	3	0	0	90	234	540	920	1492	1740	2000	2120	2160	1930	1750	1570	1240
389	1	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
390	0	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
391	1	0	1	0	0	0	0	0	0	0	0	0	2	0	0	30	113	271	510	830	1100	1230	1300	1300	1210	1045	915	755
392	1	0	1	0	0	0	0	0	0	0	0	0	2	0	0	30	113	271	510	830	1100	1230	1300	1300	1210	1045	915	755
393	0	0	0	1	1	0	0	0	0	0	0	0	1	0	0	35	91	210	350	560	630	700	700	700	595	525	455	350
394	1	1	1	1	0	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
395	0	0	1	1	1	1	0	0	0	0	0	0	3	0	0	65	169	390	670	1092	1290	1500	1620	1660	1505	1375	1245	990
396	1	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
397	1	1	1	1	1	0	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
398	1	1	1	1	1	0	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
399	1	1	1	0	1	0	0	0	0	0	0	0	4	0	0	90	269	631	1130	1842	2300	2630	2820	2860	2630	2345	2095	1695
400	1	0	1	1	1	1	0	0	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
401	0	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
402	0	1	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590
403	0	1	1	1	0	1	0	0	0	0	0	0	2	0	0	90	234	540	900	1440	1620	1800	1800	1800	1530	1350	1170	900
404	1	0	1	0	1	1	0	0	0	0	0	0	3	0	0	30	113	271	530	882	1220	1430	1620	1660	1610	1445	1315	1095
405	0	0	1	0	1	1	0	0	0	0	0	0	2	0	0	30	78	180	320	532	660	800	920	960	910	850	790	640
406	1	0	1	0	1	0	0	0	0	0	0	0	3	0														



Sheet1

411	0	1	1	0	0	0	0	0	0	0	0	2	0	0	90	234	540	900	1440	1620	1800	1800	1800	1530	1350	1170	900
412	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
413	1	1	1	1	1	0	0	0	0	0	0	4	0	0	65	204	481	880	1442	1650	2130	2320	2360	2205	1970	1770	1445
414	1	1	0	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
415	1	1	0	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
416	0	1	0	1	0	0	0	0	0	0	0	2	0	0	95	247	570	950	1520	1710	1900	1900	1615	1425	1235	950	
417	1	1	1	0	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
418	0	0	1	1	1	0	0	0	0	0	0	3	0	0	65	169	390	670	1092	1290	1500	1620	1660	1505	1375	1245	990
419	1	0	0	1	0	0	0	0	0	0	0	2	0	0	35	126	301	560	910	1190	1330	1400	1400	1295	1120	980	805
420	1	1	0	1	1	1	0	0	0	0	0	4	0	0	95	282	661	1180	1922	2390	2730	2920	2960	2715	2420	2160	1745
421	1	0	1	1	0	0	0	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
422	1	1	1	1	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
423	1	1	1	1	0	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
424	1	1	1	1	0	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
425	1	1	0	0	0	0	0	0	0	0	0	2	0	0	60	191	451	810	1310	1640	1830	1900	1900	1720	1495	1305	1055
426	0	0	1	0	0	0	0	0	0	0	0	1	0	0	30	78	180	300	480	540	600	600	600	510	450	390	300
427	1	1	0	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
428	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
429	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	35	91	210	350	560	630	700	700	595	525	455	
430	0	0	0	1	1	0	0	0	0	0	0	2	0	0	65	169	390	670	1092	1290	1500	1620	1660	1505	1375	1245	990
431	0	0	1	1	1	0	0	0	0	0	0	3	0	0	30	113	271	510	830	1100	1230	1300	1300	1210	1045	915	755
432	1	0	1	0	0	0	0	0	0	0	0	2	0	0	0	0	0	20	52	120	200	320	360	400	400	400	340
433	0	0	0	0	0	0	0	0	0	0	0	1	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650
434	0	0	1	1	0	0	0	0	0	0	0	2	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
435	1	0	1	1	0	0	0	0	0	0	0	3	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705
436	1	1	1	1	0	0	0	0	0	0	0	4	0	0	35	91	210	350	560	630	700	700	595	525	455	350	
437	0	0	0	1	0	0	0	0	0	0	0	1	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
438	1	1	1	0	0	0	0	0	0	0	0	3	0	0	90	234	540	900	1440	1620	1800	1800	1530	1350	1170	900	
439	0	1	1	1	0	0	0	0	0	0	0	2	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
440	1	1	1	1	1	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
441	0	1	1	1	0	0	0	0	0	0	0	3	0	0	35	91	210	350	560	630	700	700	595	525	455	350	
442	0	0	0	1	0	0	0	0	0	0	0	1	0	0	90	269	631	1130	1842	2300	2630	2820	2860	2630	2345	2095	1695
443	1	1	1	0	1	0	0	0	0	0	0	4	0	0	95	247	570	950	1520	1710	1900	1900	1615	1425	1235	950	
444	0	1	0	1	0	0	0	0	0	0	0	2	0	0	95	247	570	950	1520	1710	1900	1900	1615	1425	1235	950	
445	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
446	1	1	0	0	0	0	0	0	0	0	0	2	0	0	60	191	451	810	1310	1640	1830	1900	1900	1720	1495	1305	1055
447	0	1	1	1	1	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
448	1	1	1	1	0	0	0	0	0	0	0	4	0	0	90	269	631	1130	1842	2300	2630	2820	2860	2630	2345	2095	1695
449	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
450	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
451	1	1	0	0	0	0	0	0	0	0	0	2	0	0	60	191	451	810	1310	1640	1830	1900	1900	1720	1495	1305	1055
452	1	1	0	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
453	0	0	0	1	1	0	0	0	0	0	0	2	0	0	35	91	210	370	612	750	900	1020	1060	995	925	855	690
454	0	1	0	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
455	0	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2625	2275	2025	1590
456	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
457	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
458	0	1	0	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
459	0	1	0	1	0	0	0	0	0	0	0	2	0	0	95	247	570	950	1520	1710	1900	1900	1615	1425	1235	950	
460	1	0	1	1	1	0	0	0	0	0	0	4	0	0	65	204	481	880	1442	1850	2130	2320	2360	2205	1970	1770	1445
461	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
462	0	1	1	1	0	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2125	1875	1625	1250	
463	1	1	1	0	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355
464	0	1	1	1	1	0	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2625	2275	2025	1590
465	0	1	0	1	1	0	0	0	0	0	0	3	0	0	95	247	570	970	1572	1830	2100	2220	2260	2015	1825	1635	1290
466	1	0	1	1	1	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105
467	1	1	1	1	1	0	0	0	0	0	0	5	0	0	125	360	841	1480	2402	2930	3330	3520	3560	3225	2870	2550	2045
468	0	1	1	0	0	0	0	0	0	0	0	2	0	0	90	234	540	900	1440	1620	1800	1800	1530	1350	1170	900	
469	1	1	0	1	0	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405
470	0	1	0	1	0	0	0	0	0	0	0	2	0	0	95	247	5										

Sheet1

473	0	0	1	1	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650								
474	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0									
475	1	0	1	0	0	0	0	0	0	0	2	0	0	30	113	271	510	830	1100	1230	1300	1300	1210	1045	915	755								
476	1	1	1	0	0	0	0	0	0	0	3	0	0	90	269	631	1110	1790	2180	2430	2500	2500	2230	1945	1695	1355								
477	0	0	1	1	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650								
478	1	0	1	0	1	0	0	0	0	0	3	0	0	30	113	271	530	882	1220	1430	1620	1660	1610	1445	1315	1095								
479	0	1	1	0	0	0	0	0	0	0	2	0	0	90	234	540	900	1440	1620	1800	1800	1800	1530	1350	1170	900								
480	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705								
481	1	0	1	0	1	0	0	0	0	0	3	0	0	30	113	271	530	882	1220	1430	1620	1660	1610	1445	1315	1095								
482	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705								
483	0	0	1	1	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650								
484	1	0	0	1	1	0	0	0	0	0	3	0	0	35	126	301	580	962	1310	1530	1720	1760	1695	1520	1380	1145								
485	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705								
486	1	0	0	1	0	0	0	0	0	0	2	0	0	35	126	301	560	910	1190	1330	1400	1400	1295	1120	980	805								
487	1	1	0	1	1	0	0	0	0	0	4	0	0	95	282	661	1180	1922	2390	2730	2920	2960	2715	2420	2160	1745								
488	0	1	0	0	1	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650								
489	0	0	1	1	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650								
490	1	1	0	1	0	0	0	0	0	0	3	0	0	95	282	661	1160	1870	2270	2530	2600	2600	2315	2020	1760	1405								
491	0	0	1	1	0	0	0	0	0	0	2	0	0	65	169	390	650	1040	1170	1300	1300	1300	1105	975	845	650								
492	0	0	1	0	0	0	0	0	0	0	1	0	0	30	78	180	300	480	540	600	600	600	510	450	390	300								
493	1	1	1	1	0	0	0	0	0	0	4	0	0	125	360	841	1460	2350	2810	3130	3200	3200	2825	2470	2150	1705								
494	0	1	1	1	0	0	0	0	0	0	3	0	0	125	325	750	1250	2000	2250	2500	2500	2500	2125	1875	1625	1250								
495	0	1	1	1	1	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590								
496	0	0	1	0	1	0	0	0	0	0	2	0	0	30	78	180	320	532	660	800	920	960	910	850	790	640								
497	1	0	0	1	0	0	0	0	0	0	2	0	0	35	126	301	560	910	1190	1330	1400	1400	1295	1120	980	805								
498	0	1	0	0	1	0	0	0	0	0	2	0	0	60	156	360	620	1012	1200	1400	1520	1560	1420	1300	1180	940								
499	1	0	1	1	0	0	0	0	0	0	3	0	0	65	204	481	860	1390	1730	1930	2000	2000	1805	1570	1370	1105								
500	0	1	1	1	1	0	0	0	0	0	4	0	0	125	325	750	1270	2052	2370	2700	2820	2860	2525	2275	2025	1590								
250												303	350	355	188	0	0	0	0	0	0	2.892												
													400	400	400	400	400	400	400	400	400	400	400	400	400	400								
													1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000								
													9,999	9,999	9,999	9,999	9,999	9,999	9,999	9,999	9,999	9,999	9,999	9,999	9,999	9,999								
													99,999	99,999	99,999	99,999	99,999	99,999	99,999	99,999	99,999	99,999	99,999	99,999	99,999	99,999								
													8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%								
													4%	4%	4%	4%	4%	4%	4%	4%	4%	4%	4%	4%	4%	4%								
													1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%								
													0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%								
													-50	-50	-50	-50	0	0	0	0	0	0	0	0	0	0								
-0.5	-0.05	0	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05								
8	-50%										10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28								
0	-5%	Median	20.4%								22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55								
0	0%	Mode	22.9%								22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95								
5	5%	Mean	17.9%								16%	-50	-50	-45.2	-37.52	28.8	40	54.4	56.8	58	58	58	56.2	52	47.2	40								
17	10%	Min	-100.0%								23%	-50	-50	-42.4	-27.44	42.44	57.8	65.22	69.9	73.3	75.2	75.6	73.15	70.2	67.6	63.45								
25	15%	Max	24.9%								17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42								
175	20%	Std. Dev.	15.7%								25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05								
270	25%										22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05								
0	30%										20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54								
0	35%										10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28								
0	40%										16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	56.45	52.6	46.2									
											23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5								
											22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05								
											9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24								
											-100%	-50	-50	-50	-50	0	0	0	0	0	0	0	0	0	0	0								
											-100%	-50	-50	-50	-50	0	0	0	0	0	0	0	0	0	0	0								
											16%	-50	-50	-47.2	-39.92	24.08	38.4	52.4	57.9	59.3	60	60	58.95	57.2	55.2	48.2								
											25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45								

Sheet1

25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
16%	-50	-50	-47.6	-40.96	21.68	37.2	51.28	58.2	60.3	62.2	62.6	62.1	60.45	59.15	56.95
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
16%	-50	-50	-45.2	-37.52	28.8	40	54.4	56.8	58	58	58	56.2	52	47.2	40
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
0%	-50	-50	-50	-50	0	1.6	4.16	9.6	16	25.6	28.8	32	32	32	27.2
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
17%	-50	-50	-45.2	-37.52	28.8	40.8	56.12	58	60	61.2	61.6	60.2	59	57.8	53.6
-100%	-50	-50	-50	-50	0	0	0	0	0	0	0	0	0	0	0
-100%	-50	-50	-50	-50	0	0	0	0	0	0	0	0	0	0	0
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
0%	-50	-50	-50	-50	0	1.6	4.16	9.6	16	25.6	28.8	32	32	32	27.2
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
12%	-50	-50	-47.6	-43.76	14.4	25.6	37.28	42.4	48	52.8	54.4	52.4	50	47.6	41.6
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
-100%	-50	-50	-50	-50	0	0	0	0	0	0	0	0	0	0	0
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
16%	-50	-50	-47.2	-39.92	24.08	38.4	52.4	57.9	59.3	60	60	58.95	57.2	55.2	48.2
17%	-50	-50	-45.2	-37.52	28.8	40.8	56.12	58	60	61.2	61.6	60.2	59	57.8	53.6
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
16%	-50	-50	-47.2	-39.92	24.08	38.4	52.4	57.9	59.3	60	60	58.95	57.2	55.2	48.2
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54

CONFIDENTIAL  
JH 001717



Sheet1

20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
0%	-50	-50	-50	-50	0	1.6	4.16	9.6	16	25.6	28.8	32	32	32	27.2
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
23%	-50	-50	-42.4	-27.44	42.44	57.8	65.22	69.9	73.3	75.2	75.6	73.15	70.2	67.6	63.45
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
16%	-50	-50	-47.2	-39.92	24.08	38.4	52.4	57.9	59.3	60	60	58.95	57.2	55.2	48.2
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
16%	-50	-50	-45.2	-37.52	28.8	40	54.4	56.8	58	58	58	56.2	52	47.2	40
17%	-50	-50	-45.2	-37.52	28.8	40.8	56.12	58	60	61.2	61.6	60.2	59	57.8	53.6
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
17%	-50	-50	-45.2	-37.52	28.8	40.8	56.12	58	60	61.2	61.6	60.2	59	57.8	53.6
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
16%	-50	-50	-47.2	-39.92	24.08	38.4	52.4	57.9	59.3	60	60	58.95	57.2	55.2	48.2
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
20%	-50	-50	-42.8	-31.28	37.6	52.8	60.92	63.4	66	67.2	67.6	65.3	63.5	61.7	58.4
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
-100%	-50	-50	-50	-50	0	0	0	0	0	0	0	0	0	0	0
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45

CONFIDENTIAL  
JH 001718

Sheet1

20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
17%	-50	-50	-45.2	-37.52	28.8	40.8	56.12	58	60	61.2	61.6	60.2	59	57.8	53.6
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
20%	-50	-50	-45.2	-34.72	34.04	49.2	59.62	63.6	66.3	68.2	68.6	67.2	64.95	63.05	59.95
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-42.8	-31.28	37.6	52.8	60.92	63.4	66	67.2	67.6	65.3	63.5	61.7	58.4
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
16%	-50	-50	-45.2	-37.52	28.8	40	54.4	56.8	58	58	58	56.2	52	47.2	40
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
20%	-50	-50	-45.2	-34.72	34.04	49.2	59.62	63.6	66.3	68.2	68.6	67.2	64.95	63.05	59.95
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
16%	-50	-50	-47.6	-40.96	21.68	37.2	51.28	58.2	60.3	62.2	62.6	62.1	60.45	59.15	56.95
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
23%	-50	-50	-42.4	-27.44	42.44	57.8	65.22	69.9	73.3	75.2	75.6	73.15	70.2	67.6	63.45
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6

CONFIDENTIAL  
JH 001719

Sheet1

11%	-50	-50	-50	-47.2	7.28	18.4	32.08	43.2	49.2	56.2	56.6	57	55.8	53	47.8
16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
20%	-50	-50	-42.8	-31.28	37.6	52.8	60.92	63.4	66	67.2	67.6	65.3	63.5	61.7	58.4
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
17%	-50	-50	-45.2	-37.52	28.8	40.8	56.12	58	60	61.2	61.6	60.2	59	57.8	53.6
20%	-50	-50	-42.8	-31.28	37.6	52.8	60.92	63.4	66	67.2	67.6	65.3	63.5	61.7	58.4
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
20%	-50	-50	-42.8	-31.28	37.6	52.8	60.92	63.4	66	67.2	67.6	65.3	63.5	61.7	58.4
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
20%	-50	-50	-42.8	-31.28	37.6	52.8	60.92	63.4	66	67.2	67.6	65.3	63.5	61.7	58.4
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
13%	-50	-50	-47.2	-42.72	16.8	29.6	40.48	46	52	56.2	56.6	55.8	53	50.2	43.6
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
8%	-50	-50	-50	-47.2	7.28	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
17%	-50	-50	-45.2	-37.52	28.8	40.8	56.12	58	60	61.2	61.6	60.2	59	57.8	53.6
20%	-50	-50	-42.8	-31.28	37.6	52.8	60.92	63.4	66	67.2	67.6	65.3	63.5	61.7	58.4
16%	-50	-50	-47.6	-40.96	21.68	37.2	51.28	58.2	60.3	62.2	62.6	62.1	60.45	59.15	56.95
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
23%	-50	-50	-42.4	-27.44	42.44	57.8	65.22	69.9	73.3	75.2	75.6	73.15	70.2	67.6	63.45
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
13%	-50	-50	-47.2	-42.72	16.8	29.6	40.48	46	52	56.2	56.6	55.8	53	50.2	43.6
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45

CONFIDENTIAL  
JH 001720

Sheet1

17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
20%	-50	-50	-45.2	-34.72	34.04	49.2	59.62	63.6	66.3	68.2	68.6	67.2	64.95	63.05	59.95
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
20%	-50	-50	-42.8	-31.28	37.6	52.8	60.92	63.4	66	67.2	67.6	65.3	63.5	61.7	58.4
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
16%	-50	-50	-45.2	-37.52	28.8	40	54.4	56.8	58	58	58	56.2	52	47.2	40
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
23%	-50	-50	-42.4	-27.44	42.44	57.8	65.22	69.9	73.3	75.2	75.6	73.15	70.2	67.6	63.45
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
8%	-50	-50	-50	-47.2	7.28	16.8	28	38.4	41.2	44	44	39.8	37	34.2	28
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
16%	-50	-50	-45.2	-37.52	28.8	40	54.4	56.8	58	58	58	56.2	52	47.2	40
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9

CONFIDENTIAL  
JH 001721

Sheet1

20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
13%	-50	-50	-47.2	-42.72	16.8	29.6	40.48	46	52	56.2	56.6	55.8	53	50.2	43.6
16%	-50	-50	-47.2	-39.92	24.08	38.4	52.4	57.9	59.3	60	60	58.95	57.2	55.2	48.2
11%	-50	-50	-50	-47.2	7.28	18.4	32.08	43.2	49.2	56.2	56.6	57	55.8	53	47.8
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
16%	-50	-50	-47.6	-40.96	21.68	37.2	51.28	58.2	60.3	62.2	62.6	62.1	60.45	59.15	56.95
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
11%	-50	-50	-50	-47.2	7.28	18.4	32.08	43.2	49.2	56.2	56.6	57	55.8	53	47.8
0%	-50	-50	-50	-50	0	1.6	4.16	9.6	16	25.6	28.8	32	32	32	27.2
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
13%	-50	-50	-47.2	-42.72	16.8	29.6	40.48	46	52	56.2	56.6	55.8	53	50.2	43.6
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
-100%	-50	-50	-50	-50	0	0	0	0	0	0	0	0	0	0	0
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
20%	-50	-50	-42.8	-31.28	37.6	52.8	60.92	63.4	66	67.2	67.6	65.3	63.5	61.7	58.4
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2

CONFIDENTIAL  
JH 001722



Sheet1

16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
16%	-50	-50	-47.6	-40.96	21.68	37.2	51.28	58.2	60.3	62.2	62.6	62.1	60.45	59.15	56.95
12%	-50	-50	-47.6	-43.76	14.4	25.6	37.28	42.4	48	52.8	54.4	52.4	50	47.6	41.6
16%	-50	-50	-47.6	-40.96	21.68	37.2	51.28	58.2	60.3	62.2	62.6	62.1	60.45	59.15	56.95
20%	-50	-50	-45.2	-34.72	34.04	49.2	59.62	63.6	66.3	68.2	68.6	67.2	64.95	63.05	59.95
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
16%	-50	-50	-47.2	-39.92	24.08	38.4	52.4	57.9	59.3	60	60	58.95	57.2	55.2	48.2
23%	-50	-50	-42.4	-27.44	42.44	57.8	65.22	69.9	73.3	75.2	75.6	73.15	70.2	67.6	63.45
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
8%	-50	-50	-50	-47.2	7.28	16.8	28	38.4	41.2	44	44	39.8	37	34.2	28
13%	-50	-50	-47.2	-42.72	16.8	29.6	40.48	46	52	56.2	56.6	55.8	53	50.2	43.6
18%	-50	-50	-44.8	-36.48	31.2	42.8	56.92	58.9	61	62.2	62.6	61.05	59.75	58.45	55.6
18%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
0%	-50	-50	-50	-50	0	1.6	4.16	9.6	16	25.6	28.8	32	32	32	27.2
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
10%	-50	-50	-47.2	-42.72	16.8	28	38.4	41.2	44	44	44	39.8	37	34.2	28
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
22%	-50	-50	-42.8	-28.48	41.24	57.3	64.42	69	72.3	74.2	74.6	72.3	69.45	66.95	62.95
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
19%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
19%	-50	-50	-45.2	-34.72	34.04	48.4	59.1	62.4	64.3	65	65	63.2	60.95	59.05	56.55
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
13%	-50	-50	-47.2	-42.72	16.8	29.6	40.48	46	52	56.2	56.6	55.8	53	50.2	43.6

CONFIDENTIAL  
JH 001723

Sheet1

21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
20%	-50	-50	-44.8	-33.68	35.24	51.2	60.42	64.5	67.3	69.2	69.6	68.05	65.7	63.7	60.45
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
21%	-50	-50	-42.4	-30.24	38.8	54.8	61.72	64.3	67	68.2	68.6	66.15	64.25	62.35	58.9
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
25%	-50	-50	-40	-21.2	49.64	60.8	70.02	75.3	79.3	81.2	81.6	78.25	74.7	71.5	66.45
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
-100%	-50	-50	-50	-50	0	0	0	0	0	0	0	0	0	0	0
16%	-50	-50	-47.6	-40.96	21.68	36.4	49.2	57	58.3	59	59	58.1	56.45	52.6	46.2
22%	-50	-50	-42.8	-28.48	41.24	57.1	63.9	67.8	70.3	71	71	68.3	65.45	62.95	59.55
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
16%	-50	-50	-47.6	-40.96	21.68	37.2	51.28	58.2	60.3	62.2	62.6	62.1	60.45	59.15	56.95
20%	-50	-50	-42.8	-31.28	37.6	52	60.4	62.2	64	64	64	61.3	59.5	57.7	52
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
16%	-50	-50	-47.6	-40.96	21.68	37.2	51.28	58.2	60.3	62.2	62.6	62.1	60.45	59.15	56.95
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
17%	-50	-50	-47.2	-39.92	24.08	39.2	54.48	59.1	61.3	63.2	63.6	62.95	61.2	59.8	57.45
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
16%	-50	-50	-47.2	-39.92	24.08	38.4	52.4	57.9	59.3	60	60	58.95	57.2	55.2	48.2
23%	-50	-50	-42.4	-27.44	42.44	57.8	65.22	69.9	73.3	75.2	75.6	73.15	70.2	67.6	63.45
20%	-50	-50	-42.4	-30.24	38.8	54	61.2	63.1	65	65	65	62.15	60.25	58.35	54
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
22%	-50	-50	-42.4	-27.44	42.44	57.6	64.7	68.7	71.3	72	72	69.15	66.2	63.6	60.05
17%	-50	-50	-44.8	-36.48	31.2	42	56.4	57.7	59	59	59	57.05	55	49.8	42
9%	-50	-50	-47.6	-43.76	14.4	24	35.2	37.6	40	40	40	36.4	34	31.2	24
25%	-50	-50	-40	-21.2	49.64	60.6	69.5	74.1	77.3	78	78	74.25	70.7	67.5	63.05
23%	-50	-50	-40	-24	46	58.5	66	68.5	71	71	71	67.25	64.75	62.25	58.5
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9
12%	-50	-50	-47.6	-43.76	14.4	25.6	37.28	42.4	48	52.8	54.4	50	47.6	41.6	
16%	-50	-50	-47.2	-39.92	24.08	38.4	52.4	57.9	59.3	60	60	58.95	57.2	55.2	48.2
17%	-50	-50	-45.2	-37.52	28.8	40.8	56.12	58	60	61.2	61.6	60.2	59	57.8	53.6
20%	-50	-50	-44.8	-33.68	35.24	50.4	59.9	63.3	65.3	66	66	64.05	61.7	59.7	57.05
23%	-50	-50	-40	-24	46	58.7	66.52	69.7	73	74.2	74.6	71.25	68.75	66.25	61.9

CONFIDENTIAL  
JH 001724



**PLs' KU**

---

**From:** Lynn C. Klotz [LynnKlotz@compuserve.com]  
**Sent:** Tuesday, June 20, 2000 6:46 PM  
**To:** Blewitt, Stephen  
**Subject:** Preliminary Abbott basket analysis

It took me less time than I thought to consolidate my notes, so here it is in the attachment. I will not do any more work, until we agree on next steps. I am a little under two days work so far.

-- Lynn



CONFIDENTIAL  
JH 003080

Confidential Property of John Hancock  
(prepared by Lynn C. Klotz, PhD)

1

## Preliminary Analysis of Abbott Drug Basket

file: abbott-bask

### General Thoughts, Ideas and Questions

*The basket is really two baskets*

Some of the drugs in the basket are well along in clinical trials and represent new but more traditional approaches to diseases. In contrast, the remaining drugs are cytostatic cancer agents for cancer, and since this is a new untried strategy for everyone, it is high risk. The risk is compounded by the fact that most are in discovery, not in clinical trials.

In our analysis, we should perhaps treat the basket as two, and come up with independent courses of action for each. The traditional drugs in the basket cover a wide range of diseases and thus reduce the risk of competitor's drugs totally shutting Abbott out.

*Some thoughts on cytostatic drugs*

There is a general clinical trials issue for cytostatic drugs: Many will enter trials in combination with conventional cytotoxic drugs and effective combinations will have to be determined empirically. Intermediate and surrogate measures of biological response will have to be developed. Regulatory agencies are grappling with the same issues.

The idea of using cytostatic drugs in combination with traditional drugs is however enormously appealing.

Do cytostatic agents reflect Abbott's major cutting-edge cancer strategy? If not, why are they being offered to Hancock?

*Precisely what is Hancock buying?*

In the areas where Abbott is still in discovery and doesn't have specific drug candidates will Hancock be buying royalty rights for all compounds, the first to enter clinical trials or the first to enter the marketplace. Rights to the first to enter the marketplace is greatly preferred, since it eliminates the risk that the drug will make it through trials. This is one way to deal with the cytostatic area where the candidates are not yet in clinical trials.

For some compounds, Abbott is conducting clinical trials for one indication, but they state that the compound has shown promise for other indications (off label or not) and diseases. It is

CONFIDENTIAL  
JH 002081

Confidential Property of John Hancock  
(prepared by Lynn C. Klotz, PhD)

2

preferable that Hancock has royalty rights for the compound itself-- that is all indications and diseases, rather than the first indication for which it is being tested in trials. .

*How do we value the technical aspects of the drug basket and competitive drugs?*

First, we might search the business press and MedLine to validate Abbott's claims and analysis for each drug in the basket. Then, for some (many?) basket drugs we should seek the opinion of one to two experts. Literature searching one basket drug is likely a four to five hour task, and may be necessary preparation to prime us with good questions for the experts. We should not need more than two hours of an expert's time. From the point of view of due diligence, experts should be retained for most of the drugs.

*How do we value sales of the drug basket?*

Estimating actual sales of drugs in the basket is difficult, but is key for deciding on the amount of investment and royalty rate. Along with clinical trials, success risk it is the other main source of risk, assuming Abbott doesn't just disappear. Abbott's sales estimates are likely all high, because they would need to be optimistic to sell the drugs/programs internally. A few ideas for schemes for estimating sales are presented below:

1) In this scheme, determine the dollar sales for the top five (ten or twenty?) drugs in each therapeutic area (disease targets), and the average sales of all drugs in that disease area. This data is likely available for many of the disease targets--and Abbott presents some data. Then assume both: optimistically, sales will reach a level of the average of the top five; and conservatively sales will reach the average of all drugs in that area--to give us a feel for the range of sales. For example, cancer and antibiotic markets are highly fragmented, so the average sales of a particular drug is likely small, perhaps less than \$100 million. The average sales of the top five drugs may also be less than \$500 million, less than half of Abbott's projected sales. Of course, we must still take into account the average probabilities that the drugs not fail in clinical trials and reach the marketplace.

2) In this scheme, we try to estimate sales, and probabilities more from "first principles." Start with Abbott's sales estimates and adjust them downward based on market risk factors. The average probabilities that the drugs ever reach the marketplace must be separately taken into account, and should be adjusted upward or downward based on clinical trials risk factors.

The clinical trials risk factors are:

- uncertainties about the targets key role in the disease (would adjust downward the probability that the drug reaches the marketplace)
- uncertainties about toxicity (would adjust probability downward)

CONFIDENTIAL  
JH 002082

Confidential Property of John Hancock  
(prepared by Lynn C. Klotz, PhD)

3

- easily defined or fuzzy clinical trial endpoints (would adjust probability upward or downward). For example, antibiotics have easy endpoints--the patient get better and no evidence of infection; cytostatic drugs have difficult to measure endpoints when in combination with traditional drugs.

We would adjust the development phase probabilities using factors  $ct_i$  which range from perhaps zero to above one. We would need to define the appropriate adjustment factors

The market risk factors are:

- number of competitors
- efficacy and side-effects of Abbott's drug vs. competitor's drugs
- cost of Abbott drug vs competitor's drugs
- market need, dire to modest

We would adjust downward Abbott's sales estimates using factors  $mr_i$  between zero and one.

Of course determining the  $ct_i$  and  $mr_i$  factors is somewhat guess work, but at the very least the effort would allow us to better focus on the issues and get some idea of value and risk of the package.

*Thoughts on the investment risk spectrum:*

- *Example of a zero risk approach:* If Hancock received a guaranteed return on its investment each year increasing yearly regardless of sales, so that the internal rate of return was significant (e.g., 15%), there would be no risk but also no upside reward. One way of receiving the return would be for it to start, for example, in 2003 and ramp up to a maximum in 2015 and decline over the next five years. Under this scenario, Abbott would be paying return from the anticipated drug sales, and Abbott would experience all the up-side and down-side. Hancock would have no risk.
- *Example of an intermediate risk approach:* Receive a guaranteed internal rate of return of for example 5% to 7% as in the above, and receive the rest of the return based on actual sales, so upside potential exists. In this model with a 7% return, one could perhaps even take Abbott's likely inflated sales estimates, since it is all upside above 7%. This removes much of the uncertainty of estimates of eventual sales.
- *Highest risk approach:* Hancock does its best to estimate what it expects for sales on the drug basket, makes the appropriate investment with an appropriate royalty rate, and receives all its return as royalty on actual sales.

*An idea for simplifying the financial calculations of appropriate investment amount and royalty rate to give an acceptable internal rate of return (IRR) to Hancock.*

CONFIDENTIAL  
JH 002083

**Confidential** Property of John Hancock  
(prepared by Lynn C. Klotz, PhD)

4

Since all the drugs in the basket which are in clinical trials are about the same phase of clinical trials (this excludes all the cytostatic agents except one) begin sales approximately between 2003-2005 and ramp up to maximum sales in approximately 2010-2013, and patents expire about 5 years later, we could use the linear IRR model developed at present only for single drugs by treating the package as a single drug, with total sales and average probability.

This will be a quick and dirty way, and likely as good as a more detailed model, to get in the range of reasonable royalty return.

**CONFIDENTIAL**  
JH 002084

Confidential Property of John Hancock  
(prepared by Lynn C. Klötz, PhD)

**Summary Profile of the Basket**

Drug	Disease Targets	Mechanism of Action	Stage of Development	Preliminary Assessment Promise/Market-risk	Projected Maximum Sales
ABT-980	benign prostatic hyperplasia (BPH)	alpha 1a adrenoceptor antagonist	phase II completed, phase III begun?	high/medium	\$700 mil. (worldwide)
ABT-627	cytostatic therapy for hormone resistant metastatic prostate cancer (PCA)	endothelin ET-1 antagonist for Eta receptor	phase II completed, phase III begun?	medium/medium	\$1,000 mil. (worldwide)
ABT-773	bacteria resistant to present antibiotics	new class of antibiotics (ketolides)	phase III?	high/low	\$1,000 mil. (worldwide)
ABT-594	diabetic neuropathic pain	cholinergic channel modulator (chCM)	phase IIa, Phase IIb about to begin	high/medium	\$1,100 mil. (worldwide)
A-254751	cytotoxic therapy for late stage breast, NSCL, ovarian, and pancreatic cancers	binds to the colchicine site on tubulin to inhibit microtubule formation	preclinical or phase I?	high/high	\$680 million (worldwide)
ABT-518	cytostatic therapy for late stage breast, NSCL, ovarian, and pancreatic cancers	matrix metallo proteinase inhibitor (MMP1)	preclinical or phase I	high/high	\$850 mil. (worldwide)
FTI	same as ABT-518	farnesyl-transferase inhibitors which block either farnesylation of RAS or RhoB	early preclinical?	high/high	\$850 mil. (worldwide)
Uro-kinase inhibitors	same as ABT-518	serine protease inhibitor	early preclinical	high/high	\$850 mil. (worldwide)

Note to table: Market risk, in this preliminary assessment is a qualitative "feel" based on uncertainties in technical strategy, uncertainties in clinical trials, perceived value of the drug compared to others, number of competitors.

**CONFIDENTIAL**  
**JH 002085**



Confidential Property of John Hancock  
(prepared by Lynn C. Klotz, PhD)

6

Issues, Questions, Evaluation Tasks

*ABT-980 (alpha 1a adrenoceptor antagonist for BPH).*

Product is scheduled to begin Phase III clinical trials in second quarter 2000. Has it begun Phase III? What were the results of Phase II?

According to Abbott, uroselective agents such as Tamsulosin (Flomax®) and ABT980 are predicted to be the standard of care replacing existing non-selective agents. We should search the literature for a confirmation of that statement, and understand the medical communities view of selective vs non-selective agents and competitor potential of Flomax.

At time of ABT980 launch, Abbott expects competition from several other alpha 1a blockers. Abbott lists three key competitive drugs in clinical trials, one lead competitor/drug is Yamanuchi/Glaxo's drug Dutasteride which is in Phase III trials. As a "spot check," we should learn what we can about the status and promise of that drug?

*ABT 627 (endothelin ET-1 antagonist for Eta receptor for metastatic prostate cancer).*

Abbott classifies this drug as a cytostatic agent not a cytotoxic agent, because it only retards progression of PCa and doesn't cure it. Abbott is positioning it as a drug that delays progression and improves quality of life for HRPc patients. In clinical trials, quality of life is a somewhat fuzzy endpoint, but some measure can be achieved. Since prostate cancer usually progresses slowly, measuring a delay in progression may be difficult in clinical trials? What effect will this have on FDA's assessment?

Has the drug yet entered Phase III trials, if so when? Are preliminary data available? Is it the only Abbott cytostatic agent in advanced clinical trials?

The drug is in Phase I trials for other cancer types. Animal studies (Abbott's or general literature knowledge?) indicate that there is potential for other non-cancer conditions? Would Hancock receive royalties for these too; put another way, is Hancock buying royalty shares for all sales of the compound, or for just prostate cancer?

For advanced PCa, hormone therapy is the main treatment, but treatment becomes ineffective after two to three years with reduced life expectancy of only 12 months, and no chemotherapy has shown promise for these patients. Perhaps we should "spot-check" the accuracy of these statements. (Patients resistant to hormone therapy are called HRPc.)

Novatrone (Novantrone/Immunex) is the only drug for HRPc with pain. We should perhaps ascertain its promise as a competitor, as a "spot-check" on Abbott's reasoning.

CONFIDENTIAL  
JH 002086

Confidential Property of John Hancock  
(prepared by Lynn C. Klotz, PhD)

7

Are there enough HRPc patients to justify Abbott's \$1 billion projected sales of the drug, especially since there are at least 10 competitive drugs in advanced clinical trials? How will PSA testing eventually reduce the number of patients with metastatic disease? I believe it has a great success in the US.

*ABT-773 (a new class of antibiotics for bacteria resistant to present antibiotics)*

We should MedLine and business database search ketolide antibiotics to independently determine their promise. Then an expert like Stuart Levy should be consulted. Andy Onderdonk might also be able to supply the names of experts for us.

Phase II clinical trial results look impressive to me: highly efficacious against four bacteria. Why did they pick those four bacteria? Since the multicenter phase II clinical trials were completed in April 1999 and the data have been analyzed, the drug should be in phase III. Is it? How far along?

Antibiotic clinical trials are relatively straight forward, the infection disappears and the patient gets better in short time.

Adventis' ketolide (telithromycin/Ketek) is ahead with an NDA filed 3/00. Has it been approved?  
How does Abbott's ketolide compare?

*ABT-594 (cholinergic channel modulator (chCM), initial indication is for diabetic neuropathic pain).*

The drug, according to Abbott, is expected to be the first cholinergic channel modulator on the market. How promising is this approach compared to others? We should look at the phase IIa results.

There may be a problem with the therapeutic window. Phase I studies indicated a maximum tolerated dose of 150 ug/day for an oral formulation. Abbott says for capsules results "suggest that higher doses can be tolerated." How much higher? Phase IIa studies suggest "a trend towards analgesic effect at 75 ug bi daily (BID). Thus, the therapeutic window may only be slightly greater than one, and about 10% of patients at 75 ug BID had a number of uncomfortable side effects such as headaches, nausea, etc. There appears to be some risk of not passing phase II clinical trials. We should perhaps get an assessment from a pain clinical-trials expert.

While the initial indication is narrowly defined as diabetic neuropathic pain, the ultimate market is for neuropathic chronic pain in general. This is an underserved market according to Abbott.

CONFIDENTIAL  
JH 002087

Confidential Property of John Hancock  
(prepared by Lynn C. Klotz, PhD)

Pregabalin/Park-Davis is in Phase III (for neuropathic pain?) and is expected to be introduced in 2001. GV 196771 Glaxo is in phase II for neuropathic and chronic pain. These appear to be serious competitors, we should learn what we can about them from the literature, and an expert assessment.

*A-254751 (binds to the colchicine site on tubulin to inhibit microtubule formation, for MDR resistant tumors)*

The drug "inhibits the *in vitro* polymerization of microtubules." Also inhibits a broad spectrum of tumor-derived human cell lines including those that are paclitaxel and doxorubicin resistant due to MDR and other phenotypes. This meets a important market need.

In animal synergic (definition?) and xenograft models, "A-254751 demonstrated impressive oral anti tumor activity."

In dogs, there have been adverse cardiovascular effects (caused by vasoconstriction?), that have not been observed in patients. Does this mean that Phase I trials are underway, completed?

Abbott states that it will thoroughly quantify the risk from vasoconstriction in humans caused by intermittent and repeated dosing of the drug. The drug may well present too big a risk to humans and not make it out of phase I. What is Abbott's current status and assessment of the drug?

There are seven competitive colchicine site ligands in development by competitors. Three have been abandoned in Phase I (not safe) and one in phase II (why?). Three are still actively being developed. This both highlights the safety risk and the promise. We need a cancer experts assessment of the safety and promise of the approach (either Peter Glazer or someone he recommends).

I am surprised that their maximum sales estimate is less than \$1 billion, as drugs that are effective and can defeat MDR should find high usage in a total cytotoxic market of over \$7 billion.

*ABT-518 (matrix metallo proteinase inhibitor program, cytostatic therapy for late stage breast, NSCL (non-small cell lung cancer), ovarian, and pancreatic cancers)*

The MMP enzymes are elevated in cancer and are associated with the ability of cancers to metastasize. Inhibitors of MMP's may suppress tumors by suppressing invasion of the cancer into the blood and they may also suppress angiogenesis. Since they don't attack the tumor cells themselves, they are called cytostatic agents and represent chronic therapy. These may be small

CONFIDENTIAL  
JH 002088

Confidential Property of John Hancock  
(prepared by Lynn C. Klotz, PhD)

9

molecule competitors to Entremed's (Folkman's lab) angiogenesis drugs.

Abbott states that there are more than 200 compounds in development for cytostatic targets.

This is a program targeting gelatinase A and gelatinase B, because Abbott claims these two MMP's are particularly important in tumor progression. We should see what the literature says about the promise of gelatinase targeting as opposed to other enzymes involved in invasion.

Would Hancock's rights extend to all MMP inhibitors developed in the program or be limited to ABT-518?

Therapeutic window of 20 in rats bodes well to the drug.

These agents have the advantage that they can be given in combination with current therapy, so the FDA may allow clinical trials on early-stage cancer patients which would expand potential market too. In addition, in my view, these add-on combination therapies have unusual promise but are high market risk because they are new.

AB518 has been tested in animals with good pharmacokinetics and toxicology.

Abbott expects sales to begin in 2006 peaking in 2012. This means the whole clinical trial process will take about 6 years which is about right for trials today. Will this drug enter Phase I this year, so that the time schedule can be met?

*FTI program (farnesyltransferase inhibitors which either block farnesylation of RAS or RhoB, cytostatic therapy for late stage breast, NSCL, ovarian, and pancreatic cancers)*

These agents appear to inhibit angiogenesis, and so are cytostatic agents.

According to Abbott, "farnesyltransferase inhibitors have demonstrated impressive anti tumor activity in preclinical models with activity equivalent to or better than that achieved with conventional cytotoxic chemotherapy given at maximal tolerated dose."

This approach is validated by the fact that there are 12 competitor drugs in development, five in clinical trials. Abbott may be late in a crowded field. Janssen Pharmaceutica/R-11577 is in Phase III and Schering-Plough/Sch66336 is in Phase II. We should learn about the promise of these two drugs, both to assess the real promise of the approach and the potency of the competition.

While Abbott is not yet in clinical trials, has it picked a promising candidate?

CONFIDENTIAL  
JH 002089

Confidential Property of John Hancock  
(prepared by Lynn C. Klotz, PhD)

10

*Urokinase inhibitor program (serine protease that activates plasminogen to plasmin which breaks down basement membrane and interstitial matrix, cytostatic therapy for late stage breast, NSCL, ovarian, and pancreatic cancers)*

Urokinase breaks down basement membrane and interstitial matrix required for tumor growth and metastasis.

Abbott's urokinase program is more advanced than competitors (at least seven competitors in preclinicals) with potency 20 fold more than nearest competitor.

Again, the number of competitors developing urokinase inhibitors validates the approach.

CONFIDENTIAL  
JH 002090

**PLs' KV**

---

**From:** Philip Deemer [phil.deemer@abbott.com]

**Sent:** Sunday, July 16, 2000 12:36 AM

**To:** Blewitt, Stephen

**Subject:** Status

Arthur Higgins wants to get final buyoff from our CEO as soon as you are done with your due diligence on the portfolio. I told him you expect to be done or largely done by the end of the week (Friday July 21). He wants us to be ready to present the specifics the week after that. We are preparing for that now. Since I'm gone this week, I'm writing to ask you a few questions about Hancock in general for background.

What is the total approximate size of Hancock's investment portfolio (\$40B ??)?

About what percent is relegated to more aggressive investment?

And about how much toward life sciences?

Are there examples of other life science investments that I can reference if necessary besides the Abbott ones?

Thank you Steve.

**CONFIDENTIAL**  
**JH 004813**

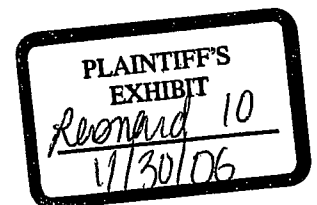


**PLs' KY**

**From:** Lynn C. Klotz [LynnKlotz@compuserve.com]  
**Sent:** Friday, July 28, 2000 10:55 AM  
**To:** Blewitt, Stephen  
**Subject:** Abbott interview writeup

See attached. Overall, most questions were answered satisfactorily--certainly no indication of any deception on Abbott's part. Only one question needs following up, the patent question on ABT-594. Let's talk to see where we go from here, and to discuss the format of the final report.

-- Lynn



**CONFIDENTIAL**  
**JH 002973**

File: interview-abbott

**Telephone Interview with Abbott, Conducted by L. Klotz (consultant) and S. Blewitt.**

Representing Abbott:

John Leonard, Vice President of Development  
Phil \_\_\_\_\_, Corporate Licensing  
Steve Cohen, Controller

**[Steve, do you have full names and formal titles for the Abbott participants?]**

Almost all answers were provided by John Leonard, as the other two Abbott participants were not scientists and this was a technically oriented interview. Interviewer questions and comments are in italics, Abbotts response in normal type.

ABT-773, ketolide antibiotic for bacteria resistant to antibiotics

*To attain a \$1 billion market for a ketolide antibiotic as Aventis predicts (and you also predict), one of the experts we interviewed thought that two things must happen. It must unseat erythromycin, and it must out compete the new fluoroquinolones which are going after the same market. Do you agree with that assessment? If so, how do you see the marketing develop for ABT-773?*

Erythromycin was unseated a decade ago, the erythromycin derivative zitromax has \$600 to \$700 US sales and over \$1 billion worldwide. It has 15% market share [*of the derivative market?*].

*[He mentioned a few other big sellers, from which it might be concluded that there is a very big total market in which Abbott could achieve a significant market share.]*

Fluoroquinolones in the past were used for urinary tract infections, but their marketers are trying to move into the respiratory infection market.

*Ketolides are related to macrolides, for which several resistance mechanisms exist. Do you expect resistance to develop rapidly from some of the minor macrolide resistance mechanisms, even though ketolides have been designed to circumvent the major efflux and ribosomal methylation mechanisms?*

In the US, efflux is the major mechanism of resistance. I believe in Japan the ribosomal mechanism may be important too. ABT-773 was originally designed and synthesized to avoid efflux. It has demonstrated efficacy on normally antibiotic resistant cells. We are about to enter Phase III trials.

*One expert stated that ketolides have a limited range of bacterial-species activity, which will*

**CONFIDENTIAL  
JH 002974**

*probably limit their usefulness to respiratory infections. While respiratory infections (sinusitis, bronchitis and pneumonia) are a very large market, do your market estimates include other large markets? If so, why do you think ABT-773 can serve those other markets?*

ABT-773 was designed first and foremost for respiratory indications.

*Your Phase II clinical data indicates a 92% effectiveness (overall eradication) against H. Influenzae. How does this compare to erythromycin? If this indicates that ABT-773 is more effective than erythromycin against H. Influenzae, how do you see that affecting market size? Can you break down the increase in market for us.*

Very early on we specifically designed our clinical trials to look at *H. Influenzae*, "which sets the bar" for these antibiotics. ABT-773 is as good or maybe better, but the study was small.

*Do you see a competitive threat from the new peptide antibiotics such as Daptinomycin?*

They are low on our radar screen, because they are IV administered. ABT-773 is for ambulatory patients, who have a cough, a stuffy nose. The IV administered antibiotics are for hospital use. We are developing an IV form of ABT-774, to compete in that market, but the market is small, and we haven't really talked too much about this.

#### ABT-594, cholinergic channel modulator for diabetic neuropathic pain

*Experts in neuropathic pain point to pregabalin (Parke-Davis, Phase III trials) as being especially promising, because it works as well as gabapentin and is safe. How does ABT-924 stack up against pregabalin? Pregabalin will likely finish clinical trials and be approved (if it is approved) before ABT-924. Although measures have been developed, pain relief is subjective, so demonstrating to the FDA that ABT-594 is more efficacious than gabapentin may be difficult. Could the difficulty of providing convincing statistics prevent the approval of ABT-924?*

We haven't compared the two drugs head-to-head, but from what we see in the pregabalin literature, we believe our drug is good. I doubt that the FDA would use pregabalin as a standard for approval. In the neuropathic pain area, there are no standards. The last drug was approved 40(?) years ago. We see no approval risk for ABT-594 from pregabalin. Also ABT-594 works through a different mechanism. There is a great need for drugs in the neuropathic pain area.

*From your descriptive memorandum, ABT-594 appears to have a therapeutic window of only two to three. Is this small therapeutic window acceptable? Has the FDA approved neuropathic pain relievers with such a low therapeutic window?*

Aspirin has a therapeutic window of only ten. For ABT-594, maybe we will be able to get a theoretical window greater than five. When we give patients the upper-limit dose, the side effects aren't dangerous: headache, vomiting. These minor side effects appear to go away over time.

*A Merck study claims that in rats "ABT-594 did not cause rotarod impairment at antinociceptive doses but did cause hypothermia and life-threatening adverse effects including seizures." This study also says its results suggest "ABT-594 has nicotine-like dependence liability....These findings indicate that the acute safety profile of ABT-594 is not significantly improved over other nicotinic analgesics." Also, Novartis finds in rats that "ABT-594 dose-dependently increased tail flick latencies but only at doses that also disrupted performance in the rotarod test" Novartis also claims "In all tests, (+)-epibatidine was significantly more potent than ABT-594." According to Abbott, ABT-594 is as efficacious as (+)-epibatidine, which is too toxic for use. How do you explain the differences between your findings in rodents and humans and the Merck and Novartis findings in rodents?*

Someone called my attention to the Merck study, I don't think I've seen the Novartis one. However, in clinical studies I would trade five million rats for a hundred people.

*Why are Merck and Novartis taking "pot shots" at you?*

I think Merck and Novartis are using us as a standard. We are the only drug to compare with. Merck bought Sybia, the company which has rights to many of the receptors like the one we are targeting.

*Is ABT-594 clear of the Sybia's patents?*

ABT-594 was prior to the Sybia/Merck arrangement. Future products must avoid Sybia's rights.

*[Note: this did not actually answer whether Abbott has an invention prior to Sybia, or if Sybia's patents may cover the receptor for Abbott's drug. We should clarify this.]*

*In an Abbott year 2000 study in rats, ABT-627 (the advanced prostate cancer cytostatic and pain drug) was examined for diabetic neuropathy. How does the promise of ABT-627 compare to ABT-594 for neuropathic pain? Are the two drugs structurally related? Is Abbott heading toward clinical trials with ABT-627 for neuropathic pain?*

Yes, we have looked at ABT-627 as an analgesic, it has limited value for pain, so we won't pursue it.

ABT-627 also might be used to treat cardiovascular disease. We don't serve that market, so we won't pursue that indication for business reasons.

ABT-980, alpha 1a adrenoceptor antagonist for BPH

*In a Chinese literature study comparing selective (tamsulosin, Flomax) and non-selective (terazosin) alpha 1-adrenoceptor antagonists, tamsulosin showed better results in maximum urinary flow rate (Qmax), and average urinary flow rate (AFR). But the results, in our naive opinion, were not dramatically different. For example, AFR increased 37.5% for tamsulosin and*

*25.8% for Flomax. I know these drugs sell well, but I am not sure why.*

*In our human trials we look at flow, and we look at symptoms. Treating the symptoms is important. For example does the bladder empty completely, is urgency to urinate reduced or eliminated.*

*We have completed Phase II, clinical trials and are about to enter Phase III. Our data so far, show that ABT-980 is virtually super imposable on Flomax, maybe we are slightly better in a few areas.*

*At what point does the FDA say, OK we have a number of products on the market which are not improvements over the previous ones, we won't approve the next one because patients don't need another similar product?*

*This is an incremental product, a lot of what our industry does is incremental products. So it becomes a marketing and pricing issue. The FDA doesn't make decisions based on the number of products already on the market. In Europe, where prices are controlled, if a product is a me-too product, it can enter the market but at a lower price.*

*One literature study refers to a patient population that is responsive to alpha1-adrenoceptor antagonists. Does this mean there is a subgroup of patients that don't respond to BPH drugs targeted to alpha1-adrenoceptor? How big is this subgroup?*

*I can't answer that; on one has carried out pharmacogenetic studies. The subgroup referred to could be those whose prostate is so big, nothing short of surgery will help them.*

*A-254751, tubulin colchicine-site binding drug to inhibit microtubule formation for advanced cancers*

*One expert said, of the number of colchicine-site binding agents in preclinical and in clinical trials, combretastatin-A4 (Oxigene, Phase I trails) stands out. He said it is receiving a lot of attention because it is also an antivasular agent. How does A-254751 stack up against combrestatin?*

*I don't know.*

*A strikingly large number of colchicine-site drugs have been abandoned in clinical trials. One expert claims the older colchicine-binding drugs failed before they are too toxic. More specifically, the older drugs failed for pharmacokinetic reasons: mainly too long half-lives in the body. He further stated: what one wants are colchicine-binding drugs that get into cells quickly, do their job, and are eliminated from the body quickly. Do you agree with this assessment? What are the pharmacokinetics of A-254751? How does the drug escape MDR?*

*I can't give you the pharmacokinetic data from memory.*

CONFIDENTIAL  
JH 002977

*Could we look at it?*

Yes, I can get it for you.

*[Since A-254751 is in early stage clinical trials, the data may give us some insight about its prospects. But I am already rating this drug as only having a fair chance of FDA approval based on the fate of the other colchicine-site binding agents. I don't see that the data can change that opinion, so I withdrew the request to see it.]*

We don't know how the drug escapes the MDR mechanism.

*How does A-254751 compare to other colchicine-site binding agents regarding toxicity?*

We think the window is pretty good compared to others.

*Cytostatic drugs (except for ABT-627, the endothelin ET-1 antagonist)*

*One literature review indicated that approximately thirty angiostatic agents are undergoing clinical trials, with another fifty agents in preclinical testing. This is a crowded field. While Abbott's approaches are clearly competitive, how can Abbott achieve a large market share given the large number of competitors in the cytostatic area in general?*

I agree that for cytostatic drugs in general their may be 50 to 200 in testing. To get the market lead, get one that works. In this business, there are a number of people who start things, many more than the ones who finish.

*One expert tells us that so far the FDA has not wavered from the strict position of improved survival as the criterion for cancer drug approval. This would include longer survival and improved quality of life. They have not yet approved any drug for slower disease progression. Since cytostatic therapies don't kill tumor cells, the use of time to progression of disease seems to be the necessary clinical trials measure. What are the problems with this measure? Do you think the difficulty of measuring time to progression, lack of statistically significant evidence of longer survival, and difficulty in determining improved quality-of-life will prolong clinical trials or cause some drugs to fail to get FDA approval? How serious an issue is this?*

You set this question up too starkly. Clearly drugs that make people to live longer, as long as they maintain a quality of life, are likely to be approved. With ABT-627, we are working with the FDA to determine what is a meaningful clinical progression. We are working with the FDA every step of the way.

*For any of your cytostatic drugs, have you any data for cost utility = (long-term-cost)/(quality-life-years-saved)? In particular, if there are side-effects, quality-life-years saved may be much less than simply life-years-saved, and cost-utility may be high.*

We haven't done cost-utility precisely, but we compare favorably with other products—for

**CONFIDENTIAL**  
**JH 002978**



example, ABT-627 compares favorably with Luprolide, a chemical castration drug with sales of \$800 million. Also, Luprolide is very expensive.

*In this regard, metalloproteinase inhibitors are particularly worrisome. One of our experts stated that the metalloproteinase inhibitor BB-94 has "underwhelming" efficacy. It is toxic and causes joint problems. Additionally, one literature study finds that the metalloproteinase inhibitor Marimastat had no survival advantage when compared to chemotherapy with gemcitabine in advanced pancreatic cancer, and Abbott states that Marimastat has dose-limiting joint side-effects. To play devil's advocate, you could argue: Why should the FDA approve a drug that does not prolong a patient's life and at the same time inflicts pain? Could failure for approval of Marimastat make the approval barriers higher for follow-on drugs? What evidence do you have that gelatinase inhibitors like ABT-518 might not have the same FDA approval concerns?*

British Biotech was first with Marimastat, so it has the problems of being first. One thing Abbott has learned from Marimastat is that it is not selective enough. Abbott's metalloproteinase inhibitor avoids blocking a particular enzyme that is needed to keep joints clear. Abbott's drug does not create what we call "frozen shoulder." There is a good animal model that we use for frozen shoulder.

#### ABT-627, the endothelin ET-1 antagonist

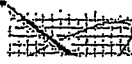
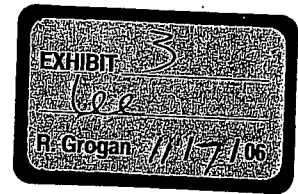
*Abbott's internal memorandum describes ABT-627 as a potent vasoconstrictor. Abbott indicated in its internal memorandum that the mechanism of action in prostate cancer wasn't yet known. Additionally, one of our experts said that reducing blood supply to tumor cells was likely not the mechanism by which ABT-627 delays prostate cancer progression, since the cancer metastasize to bone and is slow growing both indicating there is less need for a good blood supply. What are your latest thoughts about mechanism of action? A competitor who has a better knowledge of mechanism may be in good position to develop a superior drug.*

Yes, we agree that the mechanism of action for metastacized prostate cancer is not vasoconstriction. We do have knowledge about mechanism for prostate cancer.

*[The interview ended here because Steve Cohen had an important meeting to attend. There was little need for additional questions on ABT-627 as well.]*

**CONFIDENTIAL**  
**JH 002979**

**PLs' LC**

 Philip M Deemer

08/17/2000 08:50 AM

To: sblewitt@jhancock.com  
Subject: Draft Agreement

I changed my mind about getting the Draft Agreement to you. While we still do not have final approval from our CEO, I thought it prudent that we get ready to implement as soon as practical after our internal reviews. Of course there is still risk that this arrangement may not be approved by our CEO.



John Hancock Res. Prog. Agmt 3.w John Hancock Res. Prog. Agmt 3.d

CONFIDENTIAL  
AL 000138

08/17/00 DRAFT

RESEARCH FUNDING AGREEMENT

This Research Funding Agreement is made as of \_\_\_\_\_, 2000, by and between Abbott Laboratories, an Illinois corporation ("Abbott"), with its principal offices at 100 Abbott Park Road, Abbott Park, Illinois 60064-6049, and John Hancock Life Insurance Company, a \_\_\_\_\_ corporation ("John Hancock"), with its principal offices at \_\_\_\_\_.

WITNESSETH

WHEREAS, Abbott is a global healthcare company actively engaged in the research and development of human pharmaceutical products;

WHEREAS, Abbott is interested in obtaining additional funding to support such research and development activities with respect to certain pharmaceutical products which are under development;

WHEREAS, John Hancock is interested in providing such additional funding in exchange for the right to receive future milestone and royalty payments from Abbott.

NOW, THEREFORE, in consideration of the foregoing and the mutual covenants and undertakings contained herein, the parties hereto agree as follows:

ARTICLE I

DEFINITIONS

In addition to the other terms defined elsewhere herein, the following terms shall have the following meanings when used in this Agreement (and any term defined in the singular shall have the same meaning when used in the plural and vice versa, unless stated otherwise):

1.1 "Affiliate" shall mean, with respect to each party, any corporation or other form of business organization, which directly or indirectly owns, controls, is controlled by, or is under common control with, such party. An entity shall be regarded as being in control of another

CONFIDENTIAL  
AL 000139

- 2 -

entity if the former entity has the direct or indirect power to order or cause the direction of the policies of the other entity whether (i) through the ownership of fifty percent (50%) or more in the United States, or thirty percent (30%) or more outside the United States, of the outstanding voting securities (or other ownership interest for a business organization other than a corporation) of that entity; or (ii) by contract, statute, regulation or otherwise.

1.2 "Aggregate Spending Target" shall mean Six Hundred Twenty Million dollars (\$620,000,000)

1.3 "Annual Research Plan" shall mean, with respect to each Program Year during the Program Term, a reasonably detailed statement of Abbott's objectives, activities, timetable, FTE allocation and budget for its research and development activities related to the Program Compounds. The Annual Research Plan for the first Program Year shall be attached as Exhibit 1.3 within ninety (90) days of the Execution Date.

1.4 "Annual Minimum Spending Target" for each Program Year shall mean the sum of (i) the Program Payment from John Hancock for such Program Year, (ii) Fifty Million Dollars (\$50,000,000); and (iii) any Annual Carryover Amount for such Program Year pursuant to Section 3.3.

1.5 "Combination Product" shall mean a product which contains one or more Program Compounds combined as a single pharmaceutical product with one or more other therapeutically active ingredients.

1.6 "Commercially Reasonable Efforts" shall mean efforts which are consistent with those used by other pharmaceutical companies with respect to other pharmaceutical products under development which are of comparable commercial value and market potential at a similar stage of development or product life, taking into account, without limitation, issues of safety and

- 3 -

efficacy, product profile, other competitive products in the marketplace or under development, proprietary status, the regulatory environment, the status of the product and other relevant scientific factors.

1.7 "Confidential Information" shall have the meaning set forth in Section 10.2.

1.8 "Dollars" or "\$" means United States dollars.

1.9 "Execution Date" shall mean the date set forth in the introductory paragraph to this Agreement.

1.10 "FDA" shall mean the U.S. Food and Drug Administration or any successor entity thereto.

1.11 "FTE" shall mean the time and work output equivalent to one year of a full time employee who is proficient in the performance of all assigned duties and responsibilities.

1.12 "First Commercial Sale" shall mean the first sale of a Product in a given country by Abbott, its Affiliates or licensees to an unrelated third person after Regulatory Approval has been granted in such country.

1.13 "International Territory" shall mean all areas of the world outside the U.S. Territory.

1.14 "Losses" shall mean any liabilities, costs, damages, judgments, settlements and other reasonable expenses (including attorney fees).

1.15 "NDA" shall mean a New Drug Application filed with the FDA for the purpose of obtaining Regulatory Approval of a Product in the United States.

1.16 "Net Sales" shall mean:

- (a) the total gross sales of the Products (as set forth on the invoices for such sales) by Abbott, its Affiliates and licensees to third parties in any given

CONFIDENTIAL  
AL 000141

- 4 -

calendar quarter or calendar year, plus if applicable, the value of all properties and services received in consideration of a sale of products by Abbott, its Affiliates and licensees to third parties during such calendar year, less the following deductions directly paid or incurred by Abbott, its Affiliates or licensees with respect to the sale of the Products:

- (i) discounts, credits, rebates, allowances, adjustments, rejections, recalls and returns;
  - (ii) price reductions or rebates, retroactive or otherwise, imposed by government authorities;
  - (iii) sales, excise, turnover, inventory, value-added and similar taxes assessed on the royalty-bearing sale of Products;
  - (iv) transportation, importation, insurance and other handling expenses directly chargeable to the royalty-bearing sale of Products;
  - (v) chargebacks granted to drug wholesalers;
  - (vi) management fees paid to group purchasing organizations that relate specifically to the royalty-bearing sale of Products;
- (b) With respect to a Product which is sold together with any other products and/or services in a country at a unit price, whether packaged together or separately (a "Bundled Product"), the Net Sales of such Bundled Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a) above, and then the Net Sales of such Product shall be determined on a country-by-country basis as follows:



- 5 -

- (i) multiply the Net Sales of such Bundled Product by the fraction  $A/(A+B)$  where A is the average selling price of such Product in such country when sold separately and B is the total average selling price in such country of such other product(s) and/or service(s) in such Bundled Product when sold separately; or
  - (ii) if either the average selling price of such Product or the total average selling price of such other products and/or services in such Bundled Product is not available as of such date, multiply the Net Sales of such Bundled Product by a percentage determined by the mutual agreement of the Parties, which represents the proportionate economic value of such Product relative to the economic value contributed by the other products and/or services in such Bundled Product.
- (c) With respect to a Combination Product, then Net Sales of such Combination Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Combination Product shall be determined on a country-by-country basis as follows:
  - (i) Multiply the Net Sales of such Combination Product by the fraction  $A/(A+B)$ , where A is the total of the average selling prices of such Collaboration Compounds, when sold separately as a pharmaceutical product in such country and B is the total of the

- 6 -

average selling price of each other active ingredient when sold alone as a pharmaceutical product in such country; or

- (ii) if either the average selling price of all Collaboration Compounds in such Combination Product or the average selling price of all other active ingredients in such Combination Product is not available, multiply the Net Sales of such Combination Product by a percentage in a given country, determined by mutual agreement of the Parties, which represents the proportionate economic value of all Collaboration Compounds in such Combination Product relative to the economic value contributed by all other active ingredients in such Combination Product relative to the economic value contributed by all other active ingredients in such Combination Product.

- (d) For purposes of this paragraph (d), a "Premium Delivery System" means any delivery system comprising a device(s) equipment, instrumentation or other components (but not solely containers or packaging) designed to assist in the administration of a Product, such as the Abbott ADD-Vantage® System. With respect to a Product which is sold in a Premium Delivery System (a "Delivery System Product"), the Net Sales of such Delivery System Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Product shall be determined on a country-by-country basis as follows:

CONFIDENTIAL  
AL 000144

- 7 -

- (i) if the Product is sold separately without the Premium Delivery System, reduce the Net Sales of such Delivery System Product by the amount that the average selling price of the Delivery System Product in such country exceeds the average selling price of such Product as sold separately in such country; or
  - (ii) if the Product is not sold separately without the Premium Delivery System, reduce Net Sales of such Delivery System Product by an amount, determined by mutual agreement of the Parties, which represents the proportionate economic value added by the Premium Delivery System.
- (e) With respect to Endothelin, if Endothelin is developed and marketed by Abbott for one or more cancer indications and one or more non-cancer indications, Net Sales shall be based upon sales of Product only for the cancer indication(s). If the product is sold with different dosage strengths for the cancer indications and non-cancer indications, Net Sales shall be calculated based on the sales of the dosage strength(s) which are approved by the FDA for the treatment of cancer. If any dosage strength is the same for one or more cancer indications and one or more non-cancer indications, the Parties shall mutually agree to a formula, based upon IMS or other market research data, that allocates the sales of such dosage strength between the cancer indication(s), which would be included as part of Net Sales, and the non-cancer indication(s) which would be excluded from Net Sales.

CONFIDENTIAL  
AL 000145

- 8 -

1.17 "Phase I Clinical Trial" shall mean those clinical trials which utilize a limited number of human beings to preliminarily address safety and to determine what doses can be safely tolerated.

1.18 "Phase II Clinical Trial" shall mean those controlled clinical trials, the primary objective of which is to ascertain additional data regarding the safety and tolerance of one of the Program Compounds and preliminary data regarding such Program Compound's efficacy.

1.19 "Phase III Clinical Trial" shall mean one or a series of controlled pivotal studies of a specific Product by administration of such Product to human beings where the principal purpose of such trial is to provide confirmatory safety and efficacy data necessary to support the filing for Regulatory Approval of a Product.

1.20 "Product" shall mean any human prescription pharmaceutical product containing one or more of the Program Compounds as an active ingredient, alone or in combination with other active ingredients.

1.21 "Program Compounds" shall mean the preclinical, Phase I, Phase II, and Phase III Compounds listed on Exhibit 1.21, as well as any substitute compounds added by Section 4.3, and any line extensions, new formulations, new indications and Combination Products; provided, however, that with respect to Endothelin, the field of use for such Program Compound shall be limited to the treatment of cancer.

1.22 "Program Payments" shall have the meaning given in Section 3.I.

1.23 "Program Related Costs" shall mean all direct and indirect costs and expenses which are spent by Abbott on the Research Program during a given Program Year including (i) any payments made by Abbott to John Hancock pursuant to Article 6, and (ii) any milestone and license fees paid by Abbott with respect to any Program Compound.

CONFIDENTIAL  
AL 000146

- 9 -

1.24 "Program Term" shall mean a period of four (4) Program Years.

1.25 "Program Year" shall mean a period of twelve (12) consecutive calendar months, with the first Program Year commencing on , 2000 and each subsequent Program Year commencing on the anniversary of such date.

1.26 "Quarterly Reporting Period" shall mean the calendar quarter with respect to the U.S. Territory and a fiscal quarter ending on the final day of February, May, August and November (as the case may be) for the International Territory; provided, however, that if Abbott adopts the calendar year as its fiscal year for the International Territory, then the Quarterly Reporting Period for the International Territory shall also be the calendar quarter.

1.27 "Research Program" shall mean all of Abbott's activities directed towards obtaining Regulatory Approval for the Products in the Territory, including research, development, safety and efficacy studies, clinical trials, process development, formulation work, regulatory, quality, data collection and analysis and project management.

1.28 "Regulatory Approval" shall mean: (i) with respect to the U.S. Territory, the receipt of approval from the FDA to market a Product in the United States; and (ii) with respect to the International Territory, receipt of the governmental approvals required to market a Product in a given country, including any pricing and reimbursement authorization required in such country.

1.29 "Royalty Term" shall mean, with respect to each Product in each country, a period of ten (10) years from the date of First Commercial Sale of such Product in such country.

1.30 "Territory" shall mean both the U.S. Territory and the International Territory.

1.31 "U.S. Territory" shall mean the United States of America, excluding Puerto Rico and the U.S. Virgin Islands.

CONFIDENTIAL  
AL 000147

- 10 -

## ARTICLE 2

### ANNUAL RESEARCH PROGRAM

2.1 Program Term. The Research Program shall be conducted by Abbott during the Program Term and beyond the Program Term until Abbott either abandons development or receives Regulatory Approval for each Program Compound.

2.2 Research Plan. The Research Program shall be conducted by Abbott in each Research Year in accordance with the Annual Research Plan for such Research Year. The Annual Research Plan shall be prepared by Abbott and presented to John Hancock at least sixty (60) days prior to the start of each Research Year. The Annual Research Plan for the first Research Year shall be attached as Exhibit 1.3 within ninety (90) days of the Execution Date. Abbott may modify the Annual Research Plan from time to time in order to best meet the objectives of the Research Program. Any such modifications to the Annual Research Plan shall be promptly provided to John Hancock.

2.3 Conduct of Research. Abbott shall use its Reasonable Commercial Efforts to conduct the Research Program in good scientific manner, to achieve the objectives of the Research Program efficiently and expeditiously, and to comply with all applicable laws and regulations. Notwithstanding anything in this Agreement to the contrary, Abbott does not represent, warrant or guarantee that the Research Program will be successful in whole or in part or result in the registration or commercialization of any pharmaceutical products or that any Products obtaining Regulatory Approval will be a commercial success.

2.4 Subcontracting Research. Abbott may subcontract or outsource to Affiliates, licensees, or third persons any portion of the Annual Research Plan. Any subcontracting party

CONFIDENTIAL  
AL 000148

- 11 -

shall enter into a confidentiality agreement with Abbott and shall comply with all applicable laws and regulations, including good laboratory practices, with respect to its work on the Research Program. Abbott shall supervise and be responsible under this Agreement for the work of such subcontractor on the Research Program.

2.5 Research Reports and Records. Abbott shall on an annual basis, provide John Hancock with a reasonably detailed report setting forth the status of the Research Program and the Program Related Costs expended by Abbott. Abbott shall use Commercially Reasonable Efforts to maintain complete and accurate records, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes, that fully and properly reflect all work done, results achieved and Program Related Costs expended in performance of the Research Program. The books and records related to the expenditure of Program Related Costs shall be subject to audit by John Hancock. Such audit shall occur upon reasonable notice and during normal business hours by an independent auditor selected by John Hancock and reasonably acceptable to Abbott. John Hancock and its independent auditor shall maintain such records and information of Abbott in confidence in accordance with Article 10 and shall not use such records or information except to the extent permitted by this Agreement.

### ARTICLE 3

#### RESEARCH FUNDING

3.1 John Hancock Program Payments. John Hancock shall make the following installment payment to Abbott to help support the Research Programs (the "Program Payments"):



- 12 -

<u>Payment Date</u>	<u>Payment Amount</u>
Execution Date	\$50,000,000
First Anniversary of Execution Date	\$55,000,000
Second Anniversary of Execution Date	\$55,000,000
Third Anniversary of Execution Date	\$60,000,000

Such funds shall be expended by Abbott on Program Related Costs.

3.2 Abbott Program Payments. Abbott shall spend on Program Related Costs: (i) at least the Amount of the Annual Minimum Spending Target for each Program year; and (ii) at least the Aggregate Spending Target during the Program Term. John Hancock's sole and exclusive remedies for Abbott's failure to fund the Research Program in accordance with this Section 3.2 is set forth in Sections 3.3 and 3.4.

3.3 Carryover Provisions. Abbott shall be permitted to carryover its funding obligations under Section 3.2 as follows:

- (i) If in any Program Year Abbott spends on Program Related Costs, the Program Payments provided by John Hancock for such Research Year, but does not spend the full amount of the Annual Minimum Spending Target for such Program Year, Abbott agrees to spend the difference between its expenditure on Program Related Costs for such Program Year and the Annual Minimum Spending Target for such Program Year (the "Annual Carryover Amount") in the subsequent Program Year. John Hancock's obligation to make any program payment in such subsequent Program Year, pursuant to Section 3.1, shall be deferred until that time that Abbott notifies John Hancock that it has spent the Carryover Amount in such subsequent Program Year;

CONFIDENTIAL  
AL 000150

- 13 -

- (ii) If in each Program Year Abbott spends on Program Related Costs at least the Annual Minimum Spending Target but does not expend the full amount of the Aggregate Spending Target during the Program Term, Abbott agrees to expend the difference between its expenditures for Program Related Costs during the Program Term and the Aggregate Spending Target (the "Aggregate Carryover Amount") on Program Related Costs during the subsequent fiscal year commencing immediately after the end of the Program Term. If Abbott does not spend the Aggregate Carryover Amount on Program Related Costs during such subsequent fiscal year, Abbott will refund to John Hancock one-third of the Aggregate Carryover Amount, which remains unspent by Abbott.

3.4 Termination of John Hancock's Program Payments. Unless the parties agree upon an alternative arrangement, if Abbott: (i) ceases research and development of all Program Compounds during the Program Term; (ii) does not expend the Program Payment provided by John Hancock on Program Related Costs during any Program Year; (iii) does not reasonably demonstrate in its Annual Research Plan, its intent to expend Program Related Costs during the next Program Year in excess of the Program Payment provided by John Hancock for such year; or (iv) does not reasonably demonstrate, in its updated research plan, its intent to expend Program Related Costs during the Research Term in excess of the Aggregate Spending Target, John Hancock's obligation to make any remaining Program Payments pursuant to Section 3.1 shall cease. In the case of either (i) or (ii) above, Abbott shall refund to John Hancock the Program Payment for such year minus half of the Program Related Costs actually spent by Abbott during that Program Year.

- 14 -

3.5 John Hancock's obligation shall be limited to providing the program payments set forth in Section 3.1. Abbott shall be solely responsible for funding all Program Related Costs in excess of the Program Payments from John Hancock.

3.6 Notwithstanding anything else in this Agreement, for purposes of calculating whether Abbott has spent, or is projected to have spent, Program Related Cost in excess of (i) the Annual Minimum Spending Target for the first Program Year and (ii) the Aggregate Spending Target for the Program Term, Abbott shall be entitled to include within such calculations all cost and expenses incurred on or after March 1, 2000 up to the Execution Date, which would have otherwise qualified as Program Related Costs in the event that the period from March 1, 2000 to the Execution Date had been included within the Program Term. The extension of the first Program Year for the determination of whether the Annual Minimum Spending Target and the Aggregate Spending Target are met, takes into consideration that Abbott was funding all research and development cost for the Program Compounds during the time period involved in the negotiation and execution of this Agreement.

#### ARTICLE 4

##### PRODUCT RESEARCH AND DEVELOPMENT

- 15 -

4.1 Development Responsibility. Abbott shall be solely responsible for the clinical development, government approval, manufacturing, marketing, sales and distribution of Products resulting from the Research Program. Abbott agrees to use Commercially Reasonable Efforts to pursue the clinical development, government approval, manufacturing, marketing, sales, and distribution of Products throughout the Territory. The obligations of Abbott with respect to any Product under this Article 4 are expressly conditioned upon the safety, efficacy and commercial feasibility of each Product. It is the parties' expectation that under normal circumstances Abbott will file for Regulatory Approvals in Europe within two (2) years from the date of the NDA filing in the United States and in Japan within five (5) years from such NDA filing date; provided, however, that these time frames may be extended or otherwise altered based upon unforeseen circumstances that legitimately impact such regulatory filings in such foreign jurisdictions.

4.2 Within six (6) months of obtaining Regulatory Approval for any Product in a given country, Abbott, its Affiliates or licensees shall commence to market and sell such Product in such country. Abbott's obligation to market and sell a Product shall not apply to a Product in any country if Abbott has not commenced or has ceased marketing and selling such Product in the country in question substantially due to adverse business or financial conditions caused by the regulatory authorities or other governmental authorities of such country which would cause the marketing of such Product in such country to be contrary to the financial best interests of John Hancock and Abbott, including not commencing marketing and selling in a country where the regulatory authorities have price or reimbursement approval and the price or reimbursement approval or proposed by the regulatory authorities or government authorities is unacceptable to Abbott; provided, however, that Abbott, its affiliates, or its licensees shall commence or resume

- 16 -

marketing and sale of such Product in such country as soon as reasonably practical after such adverse business or financial conditions cease to exist.

4.3 Alternative Compounds. Unless the parties agree upon an alternative arrangement, in the event Abbott divests or out-licenses a Program Compound, Abbott shall substitute an alternative compound as a substitute for the divested and outlicensed Program Compound, provided that John Hancock reasonably agrees that the alternative compound has a similar market opportunity and is in a comparable stage of development or has a better development and risk profile than the divested or outlicensed Program Compound. Upon acceptance by John Hancock, which acceptance will occur unless John Hancock notifies Abbott of its non-acceptance of such substitute compound within thirty (30) days from the date that Abbott proposes such substitute compound to John Hancock, such compound shall thereafter be treated as Program Compound.

## ARTICLE 5

### PROGRAM INVENTIONS

5.1 Ownership. All inventions, innovations, ideas, discoveries, technology, know-how, methods, data, applications and products (in each case whether or not patentable arising from the Research Program ("Program Inventions")) shall be exclusively owned by or assigned to Abbott.

5.2 Patent Prosecution and Maintenance. Abbott intends to pursue broad patent protection for discoveries and inventions made under the Research Program. Abbott shall be responsible for all costs and expenses and control all decisions related to filing for patent protection, including the preparation, filing (foreign and/or domestic), prosecution, issuance, and maintenance of patent applications or patents covering Program Inventions.

- 17 -

5.3 Enforcement. Abbott shall have the sole right and authority to enforce the Compound Patents and/or any patents arising from Program Inventions against any infringers. If Abbott initiates any patent enforcement actions or lawsuits, it shall be solely responsible for the cost and expense of such action and shall be entitled to receive all moneys recovered upon the final judgment or settlement of any lawsuit.

#### ARTICLE 6

##### PAYMENTS TO JOHN HANCOCK

6.1 Closing Fee. Within \_\_\_\_ days after the execution of this Agreement, Abbott shall pay \_\_\_\_\_ (\$\_\_\_\_\_) to John Hancock as compensation for structuring this Agreement and to reimburse John Hancock for all its fees and expenses incurred in connection with this transaction.

6.2 Management Fee. Within thirty (30) days of the start of the second, third and fourth Program Year, Abbott shall pay to John Hancock a fee in the amount of \_\_\_\_\_ (\$\_\_\_\_\_) per year as compensation for monitoring Abbott's performance of its research and development activities under the Research Program directed to the development and registration of products and for its ongoing fees and expenses incurred in connection with this transaction.

6.3 Milestone Payments. Except as hereinafter limited, Abbott shall pay the following milestone payments to John Hancock in the amounts and at the times set forth below with respect to each respective Program Compound:

- (a) One Million Dollars (\$1,000,000) shall be paid within thirty (30) days after the allowance of Abbott first Investigational New Drug application for such Program Compound;

CONFIDENTIAL  
AL 000155

- 18 -

- (b) Two Million Dollars (\$2,000,000) shall be paid within thirty (30) days after the initiation of a Phase I Clinical Trial with such Program Compound;
- (c) Three Million Dollars (\$3,000,000) shall be paid within thirty (30) days after the initiation of the first Phase II Clinical Trial with such Program Compound;
- (d) Four Million Dollars (\$4,000,000) shall be paid within thirty (30) days after the initiation of the first Phase III Clinical Trial with such Program Compound;
- (e) Five Million Dollars (\$5,000,000) shall be paid within thirty (30) days after the filing of an NDA with the FDA for such Program Compound; and
- (f) Ten Million Dollars (\$10,000,000) shall be paid within thirty (30) days after Regulatory Approval of such Program Compound in the United States.

The aggregate of milestone payments under Section 6.3(a), (b), (c), (d), and (e) for all Program Compounds shall be limited to twelve million dollars (\$12,000,000), and once such aggregate limit has been paid, no further payments shall be due and payable under Sections 6.3(a), (b), (c), (d) or (e). The aggregate of milestone payments under Section 6.3(f) for all Program Compounds shall be limited to Forty Million dollars (\$40,000,000), and once such aggregate limit has been paid, no further payments shall be due and payable under Section 6.3(f). The aggregate of milestone payments under Sections 6.3(a), (b), (c), (d) and (e) for all Program Compounds shall be limited to Three Million Dollars (\$3,000,000) during the first Program Year and shall be limited to Six Million Dollars (\$6,000,000) during the second Program Year, and once such



- 19 -

aggregate limit has been reached for a particular Program Year, no further payments shall be due under Sections 6.3(a), (b), (c), (d) and (e) for the remainder of such Program Year. Further, the milestone payments set forth in Section 6.2 will not be made more than once with respect to any given Program Compound regardless of the number of such trials, filings or approvals that may be undertaken or granted with respect to such Program Compound, including, without limitation, multiple product forms of the same Program Compounds, additional active or inactive ingredients, indications, delivery modules and/or dosage strengths. Finally, a milestone payment shall only be made with respect to a milestone achieved after the date of this Agreement. For instance, if a Program Compound is in Phase III Clinical Trials at the effective Date of this Agreement, then no milestones shall ever be paid under Sections 6.3(a), (b), (c) and (d) for such Program Compound regardless of whether the Program Compound were ever to achieve such milestones as part of a different development program for instance for a new dosage strength or new indication. Exhibit 1.21 sets forth the current stage of clinical development for each Program Compound.

## ARTICLE 7

### ROYALTIES

7.1 Royalty Rates. Subject to the limitation set forth below, Abbott shall pay to John Hancock royalties equal to the following percentages calculated on the aggregate Net Sales of all Products:

<u>Royalty Percentage</u>	<u>Annual Net Sales (in Millions) of All Products in the Territory</u>
8% of those Net Sales	up to \$400
and then 4% of those Net Sales	in excess of \$400 up to \$1,000
and then 1% of those Net Sales	in excess of \$1,000 up to \$2,000
and then .5% of those Net Sales	in excess of \$2,000

CONFIDENTIAL  
AL 000157

- 20 -

7.2 Royalty Term. The obligation to make royalty payments on a Product shall be calculated on a country-by-country basis, and shall last for the duration of the Royalty Term in each given country for such Product. Notwithstanding anything to the contrary, the obligation to make royalty payments on the Products shall not begin until the commencement of the Third Program Year and shall cease at December 31, 2014.

#### ARTICLE 8

##### ROYALTY REPORTS AND ACCOUNTING

8.1 Reports, Exchange Rates. During the term of this Agreement following the First Commercial Sale of the Product, Abbott shall furnish to John Hancock a written report within sixty (60) days of the end of each calendar quarter showing in reasonably specific detail:

- (a) the Net Sales of the Product sold by Abbott, its Affiliates and licensees in the Territory during the Quarterly Reporting Period to which the report is applicable;
- (b) the royalties payable in U.S. dollars, if any, which shall have accrued hereunder based upon the Net Sales of Products;
- (c) withholding taxes, if any, required by law to be deducted in respect of such royalties;
- (d) the dates of the First Commercial Sale of the Product in any country in the Territory during the Quarterly Reporting Period;
- (e) the exchange rates used in determining the amount of U.S. dollars.

With respect to sales of the Product invoiced in U.S. dollars, the gross sales, Net Sales, and royalties payable shall be expressed in U.S. dollars. With respect to sales of products invoiced in a currency other than U.S. dollars, the gross sales, Net Sales and royalties payable shall be

CONFIDENTIAL  
AL 000158

- 21 -

expressed in their U.S. dollar equivalent, calculated using the Inter Bank rate set forth in the International Report published by International Reports Inc. as Foreign Exchange Rates quoted in New York on the day nearest the last business day of the calendar quarter. The gross sales made outside the United States during a fiscal quarter will be reported with the gross sales made in the United States during the calendar quarter in which the last month of the fiscal quarter falls.

8.2 Audits

- (a) Upon the written request of John Hancock and not more than once in each calendar year, Abbott shall permit an independent certified public accounting firm of nationally recognized standing, selected by John Hancock and reasonably acceptable to Abbott, at John Hancock's expense, to have access during normal business hours to such of the records of Abbott as may be reasonably necessary to verify the accuracy of the royalty reports hereunder for any year ending not more than twenty-four (24) months prior to the date of such request. The accounting firm shall disclose to John Hancock only whether the records are correct or not and, if applicable, the specific details concerning any discrepancies. No other information shall be shared unless Abbott invokes the dispute resolution proceedings of Section 16.7 of this Agreement.
- (b) If such accounting firm concludes that additional royalties were owed during such period, Abbott shall have the option to invoke the proceedings of Section 16.7 below or pay the additional royalties within thirty (30) days of the date John Hancock delivers to Abbott such accounting firm's written report so concluding. The fees charged by such accounting firm

CONFIDENTIAL  
AL 000159

- 22 -

shall be paid by John Hancock; provided, however, if the audit discloses that the royalties payable by Abbott for the audited period are more than one hundred five percent (105%) of the royalties actually paid for such period, then Abbott shall pay the reasonable fees and expenses charged by such accounting firm.

- (c) Abbott shall include in each permitted license granted by it pursuant to the Agreement a provision requiring the licensee to make reports to Abbott, to keep and maintain records of sales made pursuant to such sublicense and to grant access to such records by John Hancock's accounting firm to the same extent required of Abbott under the Agreement.
- (d) All reports and payments not disputed as to correctness by John Hancock within three (3) years after receipt thereof shall thereafter conclusively be deemed correct for all purposes, and Abbott and its Affiliates and licensees shall be released from any liability or accountability with respect to such royalties and payments.

8.3 Confidential Financial Information. John Hancock shall treat all financial information subject to review under this Article 8 or under any sublicense agreement as confidential, and shall cause its accounting firm to retain all such financial information in confidence.

CONFIDENTIAL  
AL 000160

- 23 -

## ARTICLE 9

### PAYMENTS

9.1 Payment Terms. Royalties shown to have accrued by each royalty report provided for under Article 8 of this Agreement shall be due and payable on the date such royalty report is due. Payment of royalties in whole or in part may be made in advance of such due date.

9.2 Payment Method. All royalties and other payments by Abbott to John Hancock under this Agreement shall be made by bank wire transfer in immediately available funds to such account as John Hancock shall designate before such payment is due. If at any time legal restrictions in any country in the Territory prevent the prompt remittance in the manner set forth in this Section 9.2 of part or all royalties owing with respect to Product sales in such country, then the parties shall mutually determine a lawful manner of remitting the restricted part of such royalty payments so long as such legal restrictions exist.

9.3. Withholding Taxes. All amounts owing from Abbott to John Hancock under this Agreement shall be paid without deduction to account for any withholding taxes, value-added taxes or other taxes, levies or charges with respect to such amounts payable on behalf of Abbott or its sublicensees and any taxes required to be withheld on behalf of Abbott or its sublicensees in any country within the Territory; provided, however, that Abbott may deduct the amount of any taxes imposed on John Hancock which are required to be withheld or collected by Abbott or its sublicensees under the laws of any country on amounts owing from Abbott to John Hancock hereunder to the extent Abbott or its sublicensees pay to the appropriate governmental authority on behalf of John Hancock such withholding taxes. Abbott shall promptly deliver to John Hancock proof of payment of such taxes together with copies of all communications from or with such governmental authority with respect thereto.

- 24 -

9.4 Late Payments. Unless otherwise provided in this Agreement, Abbott shall pay interest to John Hancock on the aggregate amount of any payments by Abbott that are not paid on or before the date such payments are due under the Agreement at a rate per annum equal to the lesser of the prime rate of interest; as reported by \_\_\_\_\_ bank in \_\_\_\_\_, from time to time, or the highest rate permitted by applicable law, calculated on the number of days such payments is delinquent.

#### ARTICLE 10.

##### CONFIDENTIALITY

10.1 Nondisclosure Obligations. Except as otherwise provided in this Article 10, during the term of the Agreement and for a period of ten (10) years thereafter, (a) John Hancock shall maintain in confidence, and shall use only for purposes of this Agreement, information and data related to the Research Compounds or Products; and (b) John Hancock shall also maintain in confidence and use only for purposes of this Agreement all information, data and materials supplied by Abbott under this Agreement, which if disclosed in writing is marked "Confidential", if disclosed orally is promptly thereafter summarized and confirmed in writing to the other party and marked confidential, or if disclosed in some other form is marked confidential.

10.2 Permitted Disclosures. For purposes of this Article 10, information and data described in clause (a) or (b) above shall be referred to as "Confidential Information"). John Hancock may disclose Confidential Information as required by applicable law, regulation or judicial process, provided that John Hancock shall give Abbott prior written notice thereof and adequate opportunity to object to any such disclosure or to request confidential treatment thereof. The obligation not to disclose or use Confidential Information shall not apply to any part of such Confidential Information that (i) is or becomes patented, published or otherwise part of the

- 25 -

public domain other than by acts or omissions of John Hancock in contravention of this Agreement; or (ii) is disclosed to John Hancock by a third party, provided such Confidential Information was not obtained on a confidential basis by such third party from Abbott, its Affiliates or licensees; or (iii) prior to disclosure under the Agreement, was already in the possession of John Hancock, provided such Confidential Information was not obtained directly or indirectly from Abbott, its Affiliates or licensees under an ongoing obligation of confidentiality; (iv) is disclosed in a press release agreed to by both parties under Section 10.3 below.

10.3 Publicity Review. Without the prior written consent of the other party, neither party shall make any statement to the public regarding the execution and/or any other aspect of the subject matter of this Agreement or any work under the Research Program. John Hancock and Abbott shall not disclose any terms or conditions of this Agreement to any third party without the prior consent of the other party, except as set forth above in this Section 10.3 or as required by applicable law, regulation or court order. [Do we want an initial press release?]

## ARTICLE 11

### TERM AND TERMINATION

11.1 Expiration. Unless terminated earlier by agreement of the parties or pursuant to Sections 11.2 or 11.4 below, this Agreement shall expire upon termination of Abbott's obligations to pay royalties under this Agreement.

11.2 Material Breach. It is the parties' express intent that consideration shall first and foremost be given to remedying any breach of this Agreement through the payment of monetary damages or such other legal or equitable remedies as shall be appropriate under the circumstances and that there shall only be a limited right to terminate this Agreement under the

- 26 -

following circumstances as a matter of last resort. In the event that the Neutral, in accordance with the procedures set forth in Section 16.7, has rendered a ruling that a party has materially breached this Agreement, which ruling specified the remedies imposed on such breaching party for such breach (the "Adverse Ruling"), and the breaching party has failed to comply with the terms of the Adverse Ruling within the time period specified therein for compliance, or if such compliance cannot be fully achieved by such date, the breaching party has failed to commence compliance and/or has failed to use diligent efforts to achieve full compliance as soon thereafter as is reasonably possible, then the non-breaching party shall have the following rights:

- (a) where Abbott is the breaching party that failed to comply with the Adverse Ruling and where the basis for such breach is Abbott's failure to abide by a material obligation under this Agreement, John Hancock may, upon written notice to Abbott after expiration of the period to comply, terminate this Agreement;
- (b) where John Hancock is the breaching party that failed to comply with the Adverse Ruling and where the basis for such breach is John Hancock's failure to abide by a material obligation under this Agreement, Abbott may, upon written notice to John Hancock after the expiration of the period to comply, terminate this Agreement.

11.3 Effect of Expiration of Termination. Expiration or termination of this Agreement shall not relieve the parties of any obligation accruing prior to such expiration or termination. The provisions of Article 10, Article 11 and Article 12 shall survive the expiration or termination of the Agreement.



- 27 -

11.4 Bankruptcy. Either party shall have the right to terminate this Agreement by delivering sixty (60) days prior written notice to the other party in the event of the other party's bankruptcy (not to include reorganization) or insolvency, provided that applicable federal bankruptcy laws shall apply.

## ARTICLE 12

### WARRANTIES AND INDEMNITY

12.1 John Hancock Representations and Warranties. John Hancock represents and warrants that:

- (a) the execution and delivery of this Agreement and the performance of the transactions contemplated hereby have been duly authorized by all appropriate John Hancock corporation action; and
- (b) the performance by John Hancock of any of the terms and conditions of this Agreement on its part to be performed does not and will not constitute a breach or violation of any other agreement or understanding, written or oral, to which it is a party.

12.2 Abbott Representations and Warranties. Abbott represents and warrants that:

- (a) the execution and delivery of this Agreement and the performance of the transactions contemplated hereby have been duly authorized by all appropriate Abbott corporation action; and
- (b) the performance by Abbott of any of the terms and conditions of this Agreement on its part to be performed does not and will not constitute a breach or violation of any other agreement or understanding, written or oral, to which it is a party.

- 28 -

12.3 No Conflict. Abbott and John Hancock represent and warrant that this Agreement does not, and will not conflict with any other right or obligation provided under any other agreement or obligation that Abbott or John Hancock has with or to any third party.

12.4 Compliance with Law. Abbott and John Hancock each represent and warrant that it shall comply with all applicable laws, regulations and guidelines in connection with that Party's performance of its obligations and rights pursuant to this Agreement, including the regulations of the United States and any other relevant nation concerning any export or other transfer of technology, services, or products.

12.5 Disclaimers.

- (a) EXCEPT AS EXPLICITLY STATED HEREIN, ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY AND FITNESS FOR ANY PARTICULAR PURPOSE, ARE EXCLUDED.
- (b) EXCEPT AS EXPLICITLY STATED HEREIN, NEITHER PARTY WILL BE LIABLE FOR CONSEQUENTIAL, INCIDENTAL OR SPECIAL DAMAGES OF ANY NATURE ARISING FROM SUCH PARTY'S ACTIVITIES UNDER THIS AGREEMENT; *PROVIDED, HOWEVER, THAT THIS LIMITATION SHALL NOT LIMIT THE INDEMNIFICATION OBLIGATION OF SUCH PARTY UNDER SECTION 12.6 BELOW FOR CONSEQUENTIAL DAMAGES RECOVERED BY A THIRD PARTY.*

12.6 Direct Indemnity. Each party shall indemnify and hold the other party and its sublicensees harmless, and hereby forever releases and discharges the other party and its

CONFIDENTIAL  
AL 000166

- 29 -

sublicensees, from and against all claims, demands, liabilities, damages and expenses, including attorneys' fees and costs (collectively, "Liabilities") arising out of negligence, recklessness or intentional misconduct of the indemnifying party or its sublicensees in connection with the work performed by such party during the Research Program, or arising out of the manufacturing, use, storage, distribution or sale of Collaboration Compounds or Products hereunder; except in each case to the extent such Liabilities resulted from negligence, recklessness or intentional misconduct of the other party.

12.7 Procedure. A party (the "Indemnitee") that intends to claim indemnification under this Article 12 shall promptly notify the other party (the "Indemnitor") of any Liability or action in respect of which the Indemnitee or any of its sublicensees intend to claim such indemnification, and the Indemnitor shall have the right to participate in, and, to the extent the Indemnitor so desires, jointly with any other Indemnitor similarly noticed, to assume the defense thereof with counsel selected by the Indemnitor; *provided, however*, that an Indemnitee shall have the right to retain its own counsel, with the fees and expenses of such counsel to be paid by the Indemnitee, if representation of such Indemnitee by the counsel retained by the Indemnitor would be inappropriate due to actual or potential differing interests between such Indemnitee and any other party represented by such counsel in such proceedings. The indemnity obligation in this Article 12 shall not apply to amounts paid in settlement of any loss, claim, damage, liability or action if such settlement is effected without the consent of the Indemnitor, which consent shall not be withheld unreasonably. The failure to deliver notice to the Indemnitor within a reasonable time after the commencement of any such action, if prejudicial to its ability to defend such action, shall relieve such Indemnitor of any liability to the Indemnitee under this Article 12, but the omission so to deliver notice to the Indemnitor will not relieve it of any liability that it may

- 30 -

have to any Indemnitee otherwise than under this Article 12. The Indemnitee, its employees and agents, shall cooperate fully with the Indemnitor and its legal representatives in the investigation of any action, claim or liability covered by indemnification under this Article 12.

12.8 Insurance. Abbott shall maintain, through self-insurance or otherwise, product liability insurance with respect to the development, manufacture and sale of Products in such amount as Abbott customarily maintains with respect to its other products. Abbott shall maintain such insurance for so long as it continues to develop, manufacture or sell any Products, and thereafter for so long as Abbott maintains insurance for itself covering such manufacture or sales.

#### ARTICLE 13

##### FORCE MAJEURE

Neither party shall be held liable or responsible to the other party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party including but not limited to fire, floods, embargoes, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, acts of God or acts, omission or delays in acting by any governmental authority or the other party.

- 31 -

#### ARTICLE 14

##### ASSIGNMENT

Except as expressly provided hereunder, this Agreement may not be assigned or otherwise transferred, nor may any right or obligations hereunder be assigned or transferred by either party without the consent of the other party; *provided, however*, that either party shall be obligated to assign this Agreement and its rights and obligations hereunder in connection with the transfer or sale of all or substantially all of its business pertaining to this Agreement, or in the event of its merger or consolidation or change in control or similar transaction. Any permitted assignee shall assume all obligations of its assignor under this Agreement.

#### ARTICLE 15

##### SEVERABILITY

Each party hereby agrees that it does not intend to violate any public policy, statutory or common laws, rules, regulations, treaty or decision of any government agency or executive body thereof of any country or community or association of countries. In any term or provision of this Agreement is held to be invalid, illegal or unenforceable by a court or other governmental authority of competent jurisdiction, such invalidity, illegality or unenforceability shall not affect any other term or provision of this Agreement, which shall remain in full force and effect. The holding of a term or provision to be invalid, illegal or unenforceable in a jurisdiction shall not have any effect on the application of the term or provision in any other jurisdiction.

- 32 -

ARTICLE 16

MISCELLANEOUS

16.1 Notices. Any consent, notice or report required or permitted to be given or made under this Agreement by one of the parties hereto to the other shall be in writing, delivered personally or by facsimile (and promptly confirmed by personal delivery, U.S. first class mail or courier), U.S. first class mail or courier, postage prepared (where applicable), addressed to such other party at its address indicated below, or to such other address as the addressee shall have last furnished in writing to the addressor and (except as otherwise provided in this Agreement) shall be effective upon receipt by the addressee.

If to John Hancock: \_\_\_\_\_

Attention: \_\_\_\_\_

copy to: \_\_\_\_\_

If to Abbott:

Abbott Laboratories  
Dept. 309, Bldg. AP30  
200 Abbott Park Road  
Abbott Park, IL 60064-3537

Attention: President, Pharmaceutical  
Products Division

copy to:

General Counsel  
Abbott Laboratories  
Dept. 364, Bldg. AP6D  
100 Abbott Park Road  
Abbott Park, IL 60064-6020

16.2 Applicable Law. The Agreement shall be governed by and construed in accordance with the laws of the State of Illinois.

CONFIDENTIAL  
AL 000170

- 33 -

16.3 Entire Agreement. This Agreement contains the entire understanding of the parties with respect to the subject matter hereof. All express or implied agreements and understandings, either oral or written, heretofore made are expressly merged in and made a part of this Agreement. This Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by both parties hereto.

16.4 Headings. The captions to the several Articles and Sections thereof are not a part of this Agreement, but are merely guides or labels to assist in locating and reading the several Articles and Sections hereof.

16.5 Independent Contractors. It is expressly agreed that John Hancock and Abbott shall be independent contractors and that the relationship between the two parties shall not constitute a partnership, joint venture or agency. Neither John Hancock nor Abbott shall have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on the other, without the prior consent of the party to do so.

16.6 Performance By Affiliates. The parties recognize that Abbott may carry out certain obligations under this Agreement through performance by the Affiliates. Abbott guarantees that the activities of its Affiliates under this Agreement shall comply with this Agreement.

16.7 Alternative Dispute Resolution. The parties shall attempt to amicably resolve disputes arising between them regarding the validity, construction, enforceability or performance of the terms of this Agreement, and any differences or disputes in the interpretation of the rights, obligations, liabilities and/or remedies hereunder, which have been identified in a written notice from one party to the other, by good faith settlement discussions between the President of Abbott's Pharmaceutical Products Division and the President and Chief Executive Officer of

CONFIDENTIAL  
AL 000171

- 34 -

John Hancock. The parties agree that any dispute that arises in connection with this Agreement, which cannot be amicably resolved by such representatives within thirty (30) days after the receipt of such written notice, shall be resolved by binding Alternative Dispute Resolution ("ADR") in the manner described in Exhibit 16.7 attached hereto.

16.8 Waiver. The waiver by either party hereto of any right hereunder or the failure to perform or of a breach by the other party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by said other party whether of a similar nature or otherwise.

16.9 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first set forth above.

JOHN HANCOCK LIFE  
INSURANCE COMPANY

ABBOTT LABORATORIES

By: \_\_\_\_\_

By: \_\_\_\_\_

Title: \_\_\_\_\_

Title: \_\_\_\_\_

CONFIDENTIAL  
AL 000172



EXHIBIT 1.3

ANNUAL RESEARCH PLAN - FIRST PROGRAM YEAR

CONFIDENTIAL  
AL 000173

EXHIBIT 1.21

PROGRAM COMPOUNDS

ABT 980 - BPH Back-up (phase III)  
ABT 627 - Prostate and other cancer (phase III)  
ABT 773 - Oral/pediatric/IV (late phase II)  
ABT 594 - Neurological/bone/acute pain (late phase II)  
E7010 - Cancer (phase II)  
ABT 518 - Cancer (phase I)  
FTI - Cancer (late preclinical)  
Urokinase - Cancer (preclinical)

EXHIBIT 16.7

ALTERNATIVE DISPUTE RESOLUTION

CONFIDENTIAL  
AL 000175

**PLs' LF**

18.10

**JOHN HANCOCK LIFE INSURANCE COMPANY**  
**Bond & Corporate Finance Group**Report Date: September 21, 2000  
Recommendation to B.I.C.: September 21, 2000  
Report to C.O.F.: October 10, 2000

Private

**Purchase Recommendation**

GBSA	\$110 mm	GBRE	\$20 mm
CLDBLK	\$ 30 mm	OPNBLK	\$ 4 mm
PENPAR	\$ 9 mm	IQA	\$15 mm
LOLA	\$ 8 mm	GRPLTC	\$ 4 mm
RETLTC	\$ 7 mm	GRPINS	\$ 2 mm
BOLI	\$ 4 mm	UNVRSL	\$ 5 mm
IPLI	\$ 2 mm		

**ABBOTT LABORATORIES ("Non-Recourse")**  
North Chicago, IL

We are recommending a \$220 million commitment to fund research and development expenses for a basket of eight pharmaceutical products ("Program Compounds") currently under development by Abbott Laboratories ("Abbott"). The commitment will be funded over a four-year period and will be subject to Abbott Laboratories co-funding at least two times our commitment on the Program Compounds during the same period of time. In return for the research and development payments, Abbott will agree to pay John Hancock milestone and royalty payments for each Compound that reaches regulatory approval and has commercial sales. The purpose of this transaction is to allow Abbott to increase its expenditures on research and development (to generate future growth in revenues and earnings) but to maintain current earnings.

The Program Compounds are a diversified pool of eight compounds owned by Abbott Laboratories and in various stages of clinical development. The Compounds are divided between late-stage and early-stage, including three Phase III, two Phase II, one Phase I, and two pre-clinical compounds. The Compounds are well-diversified from a disease/stage perspective, although several compounds are focused on the cancer market. Even within the cancer market, though, each of the Compounds targets either different types of cancer, or different mechanisms of action. Based on their current stage of development and projected sales levels, we think that the Program Compounds have a current market value of approximately \$1 billion. During the term of the transaction, we expect Abbott to spend approximately \$1.3 billion (including John Hancock's commitment) on further research and development for the Compounds.

Through the management fee and anticipated milestone payments, we expect to generate at least an 8% return on investment during the initial four years of the transaction. The average return is approximately 17.5% over 15 years. If we assume that we could sell our future royalty stream after the fifth year, our average five-year IRR would be about 22%.

The transaction is structured to provide a one-to two percent probability of total loss combined with a one-to-two percent chance of not earning a return. This is approximately equivalent to a 60 basis point annual loss over five years – or a "Ba1" credit rating. The expected return of 17.50% is attractive relative to the risk of the transaction.

**Report Authors:**Stephen J. Blewitt, Managing Director  
Scott Hartz, Managing Director  
(t:\industrials\sjb\yellowslabbott-yo3.doc)**CONFIDENTIAL**  
JH 001203

PI/Def: \_\_\_\_\_  
Exhibit No.: 10  
Witness: TUCKER  
Date: 6-27-07  
Maria A. Hasakian, CSR No. 8469



**JOHN HANCOCK LIFE INSURANCE COMPANY**

Bond &amp; Corporate Finance Group

Report Date: September 21, 2000

Recommendation to B.L.C.: September 21, 2000

Report to C.O.F.: October 10, 2000

Private

**Purchase Recommendation**

GBSA	\$110 mm	GBRE	\$20 mm
CLDBLK	\$ 30 mm	OPNBLK	\$ 4 mm
PENPAR	\$ 9 mm	IQA	\$15 mm
LOLA	\$ 8 mm	GRPLTC	\$ 4 mm
RETLTC	\$ 7 mm	GRPINS	\$ 2 mm
BOLI	\$ 4 mm	UNIVRSL	\$ 5 mm
IPLI	\$ 2 mm		

**ISSUER:** Abbott Laboratories (Non-recourse)

**ISSUE:** \$220 million Research and Development Funding Commitment

**ISSUE RATING:** JH: Ba2

**BROKER:** Direct

**SIC CODE:** 2830 - Drugs

**USE OF PROCEEDS:** To fund the research and development of eight pharmaceutical products ("Program Compounds") owned Abbott, and to pre-fund management fees and projected milestone payments, and to pay for transaction and administrative expenses.

**STATE OF INC.:** Illinois

**CIRCLE DATE:** August 31, 2000

**TAKEDOWN DATE:** Upon completion of documentation

**PROGRAM PAYMENTS:** During the Program Term, and in consideration of Abbott's continuing performance of the research services under the Research Plan, John Hancock shall make program payments to Abbott in the installments and on the dates set forth below:

<u>Date</u>	<u>Payment</u>
[December,] 2000	\$50,000,000
[December,] 2001	\$55,000,000
[December,] 2002	\$55,000,000
[December,] 2003	\$60,000,000

"Program Term" means the period commencing [December,] 2000 Date and ending on [December,] 2004.

"Research Plan" means a detailed statement of Abbott's objectives, activities, timetable, FTE allocation and budget for the Program Compounds during the Program Compounds during each year of the Program Term. Abbott shall provide an updated research plan on an annual basis.

*Abbott Obligations*

During the Program Term, Abbott agrees to spend, in addition to the funds provided by John Hancock, (i) a minimum of \$50 million per year and (ii) a minimum of \$400 million in aggregate on research and development programs associated with the Program Compounds.

*Program Payment Termination Provisions*

Unless the parties agree upon an alternative arrangement, if Abbott (a) ceases research and development of all Program Compounds or (b) does not spend at least the amount provided by John Hancock in a year on the research and development of Program Compounds or (c) does not reasonably demonstrate, in its updated research plan, its intent to spend a minimum of the amount provided by John Hancock in the next year of the Program Term or \$620 million (including the funds provided by John Hancock) in aggregate, John Hancock's obligation to continue to make Program Payments shall cease. In the case of either (a) or (b) above, Abbott will refund to John Hancock \$55 million minus half of the amount actually spent by Abbott during that year.

*Carryover Provisions*

If Abbott spends the amount provided by John Hancock in a year but does not spend at least an additional \$50 million, Abbott agrees to spend the difference between \$105 million and the amount actually spent in that year (the "Carryover Amount") in the subsequent year. John Hancock's obligation to make Program Payments in the subsequent year, if any, will be deferred until that time that Abbott demonstrates that it has spent the Carryover Amount in that subsequent year.

If Abbott spends the amount provided by John Hancock in each year and at least an additional \$50 million in each year, but does not spend a minimum of \$620 million (including the funds provided by John Hancock) in aggregate on research and development programs associated with the Program Compounds during the Program Term, Abbott agrees to spend the difference between \$620 million and the aggregate amount actually spent (the "Aggregate Carryover Amount") in the subsequent year. If Abbott does not spend the Aggregate Carryover Amount in the subsequent year, Abbott will refund to John Hancock one-third of the difference between (a) \$620 million and the amount actually spent.

**MANAGEMENT FEE:**

Commencing with the first anniversary of the Program Term and continuing until the end of the Program Term, Abbott shall pay John Hancock a fee in the amount of \$2.0 million per year as compensation for monitoring Abbott's continuing performance of its research services under the Research Plan, the development of the Program Compounds, and to reimburse John Hancock for its ongoing fees and expenses incurred in connection with this transaction.

**CONFIDENTIAL**  
**JH 001205**

**MILESTONE PAYMENTS:**

Abbott shall make the following payments for each compound for each milestone achieved after commencement of the Program Term:

Upon the allowance of an IND application by the FDA: \$1,000,000

Upon the initiation of a Phase I Clinical Trial: \$2,000,000

Upon the initiation of a Phase II Clinical Trial: \$3,000,000

Upon the initiation of a Phase III Clinical Trial: \$4,000,000

Upon the filing of an NDA application with the FDA: \$5,000,000

Upon NDA Approval by the FDA: \$10,000,000

Aggregate milestone payments paid by Abbott, for all "non-NDA Approval" milestones achieved will not exceed \$12 million. Aggregate milestone payments paid by Abbott, for all "NDA Approval" milestones achieved will not exceed \$40 million. In addition, "non-NDA Approval" milestone payments will not exceed \$3 million in the first year or \$6 million in the second year after commencement of the Program Term.

**ROYALTY PAYMENTS:**

Abbott shall pay to John Hancock royalties on aggregate worldwide Net Sales of Program Compounds (all Program Compound sales combined) at the following rates:

<u>Annualized Net Sales of Aggregate Program Compounds</u>	<u>Royalty Rate</u>
\$0 to \$400 million	8%
>\$400 million and ≤ \$1,000 million	4%
>\$1,000 million and ≤ \$2,000 million	1%
>\$2,000 million	½%

The obligation to make royalty payments shall commence on the date of the First Commercial Sale of a Program Compound and shall continue with respect to Net Sales of such Program Compound for a period of ten years. Notwithstanding the foregoing, the obligation to make royalty payments on all Program Compounds shall not begin until after the second anniversary of the Program Term and shall cease at December 31, 2014.

**HANCOCK HOLDINGS:**

None

**RELATED HOLDINGS:**

\$29,000,000 Preferred Stock of Metabolex Corporation with Put Rights to Abbott

**ANALYST:**

Stephen J. Blewitt

**HOUSE COUNSEL:**

Amy Weed

**SPECIAL COUNSEL:**

Choate, Hall & Stewart

**Report Authors:**

Stephen J. Blewitt, Managing Director

Scott Hartz, Managing Director

(t:\industrials\sjb\yellow\abbott-yo3.doc)

**CONFIDENTIAL**  
JH 001206



**TRANSACTION OVERVIEW**

In December 1999, John Hancock approached Abbott Laboratories, Inc. ("Abbott") with a financial structure that would allow Abbott to increase its research and development expenditures (to generate future growth in revenues and earnings) but maintain current earnings. The structure, which is presented in this investment recommendation, uses probability analysis on a diversified portfolio of drug compounds, supplemented by scientific due diligence, to achieve an investment grade or near investment grade risk for John Hancock and allow us to generate equity returns in the form of current (royalty) income for a sizeable investment.

This transaction requires John Hancock to commit to funding an average of \$55 million per year for a period of four years to fund the research and development of a diversified pool of eight compounds ("Program Compounds") owned by Abbott Laboratories. We have valued the Program Compounds today at approximately \$1 billion (or five times our investment) and we expect Abbott to spend over seven times our investment during the term of the transaction (during the initial four year period, Abbott will commit two times John Hancock's investment for those compounds). In return for the research and development payments, Abbott will agree to pay John Hancock milestone and royalty payments for each compound that reaches regulatory approval and has commercial sales as well as a management fee.

Through the management fee and anticipated milestone payments, we expect to generate at least an 8% return on investment during the initial four years of the transaction. The average return is approximately 17.5% over 15 years. If we assume that we could sell our future royalty stream after the fifth year, our average five-year IRR would be about 22%.

This transaction is consistent with our approach to investing in the pharmaceutical sector. During the past five years, we have invested approximately \$460 million in pharmaceutical companies. Approximately \$300 million is invested in straight debt for investment grade companies. The remaining \$160 million is invested in equity-oriented transactions where we think that there are opportunities for exceptional value. Although we have invested in a couple of straight equity transactions, approximately \$150 million of the \$160 million is invested in transactions where our downside risk is protected by either "put rights" to investment grade companies (Metabolex, Nexell), senior note positions (Celgene, Cubist), or structured portfolios of drug candidates (Pharma Marketing). In these transactions, we maintain sizable up-side potential but reduce the probability of losing all of our invested capital through the structure of our investment.

In summary, we think that the structure of this transaction, which has us co-investing with Abbott Laboratories in a diversified pool of their drug compounds, which we believe have a current value of approximately \$1 billion, over a four year period, during which time Abbott has to meet co-investment obligations and the drug compounds need to continue to progress in development, allows us to generate substantial current income that exceeds the risk associated with the transaction. Although we are committing to a substantial \$220 million investment, our expectation is that our net investment will not exceed \$176 million (due to management fees, milestone payments, and royalty payments).

The transaction is structured to provide a one-to-two percent probability of total loss combined with a one-to-two percent chance of not earning a return. This is approximately equivalent to a 60 basis point annual loss over five years – or a "Ba1" credit rating. The expected return of 17.50% is attractive relative to the risk of the transaction.

**CONFIDENTIAL**  
JH 001207

Expected accounting treatment

There have been a number of royalty streams sold off in the form of an asset backed security. The most visible example is the David Bowie bond bought by Prudential Insurance. While this royalty transaction has many similar features, it is also different in that it is funded over a four year period and no royalties are currently being generated. We believe that at the end of the funding period we will be able to obtain a rating on the transaction that will allow it to be placed on our bond schedule. In the meantime, it will appear on our BA schedule. We plan to account for this investment using the guidance in ruling 9920 of the Emerging Issues Task Force. Ruling 9920 requires that each year, or more often if the assumptions change, we will project the expected cash flows and book income equal to the internal rate of return. Any changes to the expected cash flows will be spread over the remaining life of the transaction through the newly calculated IRR. This is the same method we use to account for our CBO equity investments. Initially we expect the IRR on this investment to be approximately 17%.

**OVERVIEW OF ABBOTT LABORATORIES**

Abbott Laboratories is engaged in the discovery, development, manufacture and sale of healthcare products and services. Abbott has five reporting revenue segments: Pharmaceutical Products, Diagnostic Products, Hospital Products, Ross Products and International. It also has a 50%-owned joint venture, TAP Holdings, Inc. The principal products of the Pharmaceutical Products Division are the anti-infectives clarithromycin, agents for the treatment of epilepsy, migraine and bipolar disorder, including Depakote; urology products, including Flomax for the treatment of BPH; Abbotkinase, a thrombolytic drug, and the anti-viral Norvir, a protease inhibitor for the treatment of HIV. The Diagnostic Division's products include diagnostic systems and tests for blood banks, hospitals, and commercial laboratories. The Hospital Products Division sells drugs and drug delivery systems, intensive care products, cardiovascular products, renal products, and intravenous and irrigation solutions. The Ross Products Division sells adult and pediatric nutritionals such as Similac, Isomil, Ensure, Glucerna, and Pedialyte. The International Division's products include a broad line of hospital, pharmaceutical, and adult and pediatric nutritional products marketed and primarily manufactured outside the United States.

For the year ended December 31, 1999, Abbott had revenues and net income of approximately \$13.2 billion and \$2.4 billion, respectively. Abbott is rated "Aaa" by the major rating agencies. As of September 18, 2000, Abbott had a market capitalization of approximately \$74 billion.

**ABBOTT LABORATORIES  
CONSOLIDATED STATEMENT OF OPERATIONS**

(S in thousands)	Fiscal Years Ended December 31,		
	1997	1998	1999
Net Sales	\$11,889	\$12,512	\$13,177
Costs and expenses:			
Cost of goods sold	5,052	5,406	5,977
Selling, general and administrative	2,695	2,759	2,857
Research and development	1,307	1,228	1,193
Total operating expenses	9,055	9,395	10,028
Operating income	2,833	3,117	3,149
Net interest expense	85	102	81
Other charges	(186)	(223)	(330)
Income (loss) before taxation	2,934	3,241	3,396
Net income (loss)	\$2,079	\$2,331	\$2,445

**CONFIDENTIAL**  
JH 001208

**TRANSACTION DETAILS****A. PROGRAM COMPOUNDS**

There are eight Program Compounds included in this transaction. The Compounds are divided between late-stage and early-stage, including three Phase III, two Phase II, one Phase I, and two pre-clinical compounds. The Compounds are well-diversified from a disease/stage perspective, although several compounds are focused on the cancer market. Even within the cancer market, each of the Compounds targets either different types of cancer, or different mechanisms of action. The products are described more fully below:

Product	Indication	JH Est. Peak Sales (\$mm)	Stage of Development
ABT 980 (BPH)	Treatment of benign prostatic hyperplasia	600	Development Stage: Phase III Expected Launch: 2003
ABT 773 (Ketolide)	Antibiotic	800	Development Stage: Phase III Expected Launch: 2003
ABT 627 (Endothelin)	Treatment of prostate cancer	700	Development Stage: Phase III Expected Launch: 2003
ABT 594 (CCM)	Non-opioid, non-NSAID analgesic	700	Development Stage: Phase II Expected Launch: 2004
E7010 (Anti-mitotic)	Cancer	500	Development Stage: Phase III Expected Launch: 2004
MMPI	Cancer	400	Development Stage: Phase I Expected Launch: 2005
FTI	Cancer	400	Development Stage: Pre-clinical Expected Launch: 2005
Urokinase	Cancer	400	Development Stage: Pre-clinical Expected Launch: 2005

**B. SUMMARY OF ESTIMATED SALES**

In estimating sales projections by Program Compound, we started with determining the expected peak sales for each Compound. We have conservatively estimated the peak sales for each Compound based on our evaluation of market potential for each Compound relative to results for other similar drugs and expected competitive drugs. In general, our level of peak sales is significantly below Abbott's level (approximately 25%) -- but, because of the tiered royalty structure, the relative economic difference is not significant. Our next step was to use a Sales Curve calculated by Lehman Brothers that projects ramp-up and ramp-down for sizeable drugs. In general, this Curve shows peak sales being reached seven years after launch. Ramp-up is achieved by 5% of peak sales in the first year, followed by 13%, 25%, 50%, 80%, and 90%. Peak sales are maintained for three years, and the compound then achieves 85% of peak, 75%, 70%, etc. As expected, every compound has its own unique curve, and Lehman's is only a general estimate. We have compared the curve to IMS data of prescription sales for individual compounds in a number of drug classes from 1981 to 1999. Our analysis indicates that Lehman's curve is a good fit and we have applied that curve. The table below shows projected sales for each Compound and probability-weighted estimated sales for the entire portfolio of Compounds.

## ESTIMATED SALES PROJECTION

(\$ in millions) Name	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
<u>Projected Sales</u>												
ABT-980 (BPH)	30	78	180	300	480	540	600	600	600	510	0	0
ABT-627 (Endothelin)	35	91	210	350	560	630	700	700	700	595	0	0
ABT-773 (Ketolide)	40	104	240	400	640	720	800	800	800	680	0	0
ABT-594		35	91	210	350	560	630	700	700	700	595	0
E7010 (Anti-mitotic)		20	52	120	200	320	360	400	400	400	340	0
MMPI												
FTI			20	52	120	200	320	360	400	400	400	340
Urokinase												
Total Projected Sales	105	328	793	1,432	2,350	2,970	3,410	3,560	3,600	3,285	1,335	340
Estimated Sales	76	225	531	932	1,510	1,837	2,068	2,129	2,138	1,908	530	74

*For projection purposes, MMPI, FTI and Urokinase are considered as one Program Compound with a Phase I probability of success.*

C. MILESTONE AND ROYALTY PAYMENTS

Under the Agreement, Abbott agrees to pay to John Hancock royalties on aggregate worldwide Net Sales of Program Compounds (all Program Compound sales combined) at the following rates: 8% on the first \$400 million, 4% on the next \$600 million, 1% on the next \$1 billion, and ½% on any amount above \$2 billion. Abbott's obligation to make royalty payments will commence on the date of the First Commercial Sale of a Program Compound and will continue with respect to Net Sales of such Program Compound for a period of ten years. Notwithstanding the foregoing, the obligation to make royalty payments on all Program Compounds will not begin until after the second anniversary of the Program Term and will cease at December 31, 2014. Based on our estimate of aggregate sales for the Program Compounds, we expect the following amounts of Royalty Payments:

(\$ in millions) Name	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Estimated Sales	76	225	531	932	1,510	1,837	2,068	2,129	2,138	1,908	530	74
<u>Royalty Payments</u>												
8.0% on \$400 mm	6	18	32	32	32	32	32	32	32	32	32	6
4.0% on \$400-\$1,000	0	0	5	21	24	24	24	24	24	24	5	0
1.0% on \$1,000 - \$2,0	0	0	0	0	5	8	10	10	10	9	0	0
0.5% on \$2,000+	0	0	0	0	0	0	0	1	1	0	0	0
Total Royalty Pymts	6	18	37	53	61	64	66	67	67	65	37	6
(average percent)	8.0%	7.0%	5.7%	4.0%	3.5%	3.2%	3.1%	3.1%	3.1%	3.4%	7.0%	8.0%

CONFIDENTIAL  
JH 001210

In addition to the Royalty Payments, Abbott will be obligated to make payments to John Hancock for certain milestones achieved for each compound. The milestone and the corresponding payments are described below. Aggregate milestone payments paid by Abbott, for all "non-NDA Approval" milestones achieved will not exceed \$12 million. Aggregate milestone payments paid by Abbott, for all "NDA Approval" milestones achieved will not exceed \$40 million. In addition, "non-NDA Approval" milestone payments will not exceed \$3 million in the first year or \$6 million in the second year after commencement of the Program Term.

Upon the allowance of an IND application by the FDA:	\$ 1,000,000
Upon the initiation of a Phase I Clinical Trial:	\$ 2,000,000
Upon the initiation of a Phase II Clinical Trial:	\$ 3,000,000
Upon the initiation of a Phase III Clinical Trial:	\$ 4,000,000
Upon the filing of an NDA application with the FDA:	\$ 5,000,000
Upon NDA Approval by the FDA:	\$10,000,000

Based on the number of Compounds in the Program and the number of potential milestones for each Compound, we expect to receive \$3 million, \$6 million, and \$3 million of "non-NDA" milestone payments in the first three years. In addition, we expect to receive \$20 million in 2003 and \$10 million in 2004 for NDA Approvals.

In aggregate, the management fees, milestone payments, and royalty payments are approximately 4.3% of Net Sales of the Program Compounds. The tiered structure of the royalty payments and the up-front milestone payments, however, substantially reduce the downside of the transaction in the event that aggregate net sales are below our expected case. For example, if sales were 25% below projected, a flat 4.3% royalty rate would yield a loss ratio of 4% versus a loss ratio of 1.6% when using the tiered structure.

#### D. ESTIMATED CASH FLOW PROJECTIONS

Based on the calculations of Net Sales and Milestone and Royalty Payments, which are described above, the Cash Flow of this transaction is as presented in the table below. In particular, the structure provides for adequate current income during the first two-to-three years when there are no approved Compounds, and substantial current royalty income based on Net Sales of approved Compounds.

(S in millions)		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Name																
JH Cash Payments	(50)	(55)	(55)	(60)												
Management Fee	0	2	2	2	2											
Milestone Payments	0	3	6	23	10											
Royalty Payments	0	0	0	6	18	37	53	61	64	66	67	67	65	37	6	
Aggregate Cash Rcv'd	0	5	8	31	30	37	53	61	64	66	67	67	65	37	6	
JH Net Cash Flow	(50)	(50)	(47)	(29)	30	37	53	61	64	66	67	67	65	37	6	

The projected bond equivalent yield for this transaction is approximately 17.5% and the cash to invested capital ratio is 2.7 times.

**E. SUMMARY BUDGET**

Abbott will be using the funds from this transaction to invest in the research and development of a specific pool of drug compounds, and to pre-fund management fees and projected milestone payments. These funds will be part of a total investment by Abbott of approximately \$1,300 million during the next ten years and \$900 million over the four year co-investment period. In addition, based on the stage of the development of the Program Compounds, and their expected sales, we have valued the Program Compounds today at approximately \$1 billion. Our valuation is based on our knowledge of "out-licensing" transactions between pharmaceutical companies and the milestone and royalty structure that is market for different stage compounds. In general, out-license transactions provide the licensor with a royalty rate of between 10% (for Phase I compounds) to 30% (for Phase III compounds) and a 50/50 split for compounds that have completed Phase III. Using an average 20% royalty applied to estimated sales and a 15% discount rate, we arrived at a value of approximately \$1 billion.

The following table summarizes the Company's expected budget during the Program Period:

(\$ in millions)		2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Total
Name													
<u>Projected Budget</u>													
ABT-980 (BPH)		80	40	30	30	20	20	10	10	10	10	10	270
ABT-627 (Endothelin)		40	40	20	20	20	20	20	10	10	10	10	220
ABT-773 (Ketolide)		135	60	42	42	27	27	27	17	17	17	17	428
ABT-594		70	80	30	20	20	20	20	20	10	10	10	310
E7010 (Anti-mitotic)		20	30	35	20	30	10	10	5	5	5	5	175
MMPI		20	30	35	20	23	15	15	5	5	5	5	178
FTI		5	10	37	17	15	15	5	5	5	5	5	124
Urokinase		15	25	35	33	15	15	5	5	5	5	5	163
Total Projected Budget		385	315	264	202	170	142	112	77	67	67	67	1,868
Estimated Budget		327	250	201	134	90	81	66	45	40	40	40	1,314

CONFIDENTIAL  
JH 001212

## TRANSACTION ANALYSIS

The structure of this transaction (which includes a diversified pool of eight Abbott compounds, and a tiered royalty structure) offers a substantial likelihood that we will receive a long-term bond equivalent yield of approximately 17.5% which is substantially greater than the inherent risk of the transaction.

### Expected Return.

#### *Methodology*

Determining the fair economics of the proposed transaction is highly dependent upon the number of compounds included, the characteristics of the compounds (i.e. status of development, potential sales), the structure of the royalty rates, and an estimation of what is a fair return. To help us answer these questions, we have taken several steps. First, we have researched industry standards for likelihood of success and probable sales curves for compounds in different stages of development. Second, we have developed a spreadsheet model that calculates the rate of return for a chosen portfolio and have developed a minimum number of compounds and associated milestone/royalty payments to provide us with returns that adequately compensate us for the risk we are taking. Third, we have tried to determine what rate of return the capital markets would require for the level of risk that we are willing to take.

The Program Compounds consist of five of Abbott's late-stage development compounds and a basket of three pre-clinical cancer compounds. The late-stage compounds range from mid-Phase II to starting Phase-III. Peak annual sales for these compounds range from \$400 million to \$800 million. With the exception of the "cancer basket", the compounds are independent of each other. Our due diligence provided us with results consistent with Abbott's representations and expectations for the Program Compounds, although we have scaled back sales projections significantly.

Our scientific and market diligence for the portfolio of compounds consisted on a number of steps. As a first step, we received internal scientific and business write-ups from Abbott for each Program Compound. The material provided by Abbott demonstrated the scientific rationale for the compounds, results of clinical trials, and a competitive analysis. Through financial reports, we searched for all references to Abbott's compounds and all references to competitive compounds in the same class or same disease category. We used this information to evaluate the potential size of markets for the Program Compounds and their competitive landscape. We engaged Dr. Lynn Klotz to search the major drug and medical databases for scientific reports on the Program Compounds and competitive compounds in the same class or same disease category. We used this information to evaluate, from a scientific perspective, what research scientists had discovered about the Program Compounds from an efficacy and safety perspective. We also used this information to identify potential experts to contact for additional questions. Finally, Dr. Klotz contacted the experts on a non-disclosure basis (not revealing that we were looking at Abbott compounds) and asked the experts to assess the Program Compounds and any potential competitive products from an efficacy and market potential perspective. In summary, none of our diligence revealed any information that was materially different than what Abbott had provided to us.

Dr. Lynn Klotz is a former professor of Biochemistry and Molecular Biology at Harvard University and a former officer of two biotechnology companies, BioTechnica and Codon. Dr. Klotz is currently an independent consultant. His most recent assignment was as a member of a four-person team consulting with the President of Mississippi State University to provide a strategic plan for their Life Sciences Institute.



*Probabilities of Success*

Based on the development stage of each compound, we assigned probabilities of success ("regulatory approval") and time to success for each compound. Our probabilities of success come from a 1995 study by Dr. Joseph A. DiMasi at the Tufts Center for the Study of Drug Development, and were modified based on our specific knowledge of the Program Compounds. Dr. DiMasi's study is generally accepted by the pharmaceutical industry as an accurate assessment of the probability of success and of the time and costs associated with drug development. Dr. DiMasi looked at a random sample of 93 compounds in four broad disease categories from 12 pharmaceutical companies that were first tested in humans between 1970 and 1982.

Dr. DiMasi's results are summarized below:

**PROBABILITY OF SUCCESS**

Entering Phase	NSAID	Cardio-vascular	Anti-infective	Neuro-pharm	All
I	22%	26%	30%	20%	23%
II	30%	41%	38%	22%	31%
III	71%	72%	77%	51%	63%

Dr. DiMasi calculated the average time to approval as 8.75 years for compounds entering Phase I, 7.5 years for compounds entering Phase II, and 5.5 years for compounds entering Phase III. Embedded in these times was an approximately 30-month review process by the FDA. Due to legislative and process changes, the average FDA review time is now approximately 12 months. A revised timeframe for approval (which was been published by TCSD in 1999), based on accelerated review by the FDA, and quicker processes within the pharmaceutical companies, is 6.0 years for Phase I, 5.0 years for Phase II, and 3.0 years for Phase III.

*Sales Estimates*

In estimating sales projections by Program Compound, we started with determining the expected peak sales for each Compound. We have conservatively estimated the peak sales for each Compound based on our evaluation of market potential for each Compound relative to results for other similar drugs and expected competitive drugs. In general, our level of peak sales is significantly below Abbott's level (approximately 25%) -- but, because of the tiered royalty structure, the relative economic difference is not significant. Our next step was to use a Sales Curve calculated by Lehman Brothers that projects ramp-up and ramp-down for sizeable drugs. In general, this Curve shows peak sales being reached seven years after launch. Ramp-up is achieved by 5% of peak sales in the first year, followed by 13%, 25%, 50%, 80%, and 90%. Peak sales are maintained for three years, and the compound then achieves 85% of peak, 75%, 70%, etc. As expected, every compound has its own unique curve, and Lehman's is only a general estimate. We have compared the curve to IMS data of prescription sales for individual compounds in a number of drug classes from 1981 to 1999. Our analysis indicates that Lehman's curve is a good fit and we have applied that curve. The table below shows projected sales for each Compound and probability-weighted estimated sales for the entire portfolio of Compounds.

*Financial Model and Results*

We've modeled the returns on this portfolio of drugs using a Monte Carlo simulation and assuming their probabilities of success are independent. Let's start, however, with some simplifying assumptions to get better intuition on the risk of the transaction. Assume the probability of success of each drug is 50%, the drugs are independent, and that the success of any one drug will give us a return of 8% on the transaction. In this case, we will lose all our investment only if all the drugs fail. The probability of this is  $(1/2)^6 = 1.6\%$ . Spread over a 4 year duration, the expected annual loss is 40 basis points which implies the same risk as a Baa3 bond. If only one drug is successful, which should occur with the probability of  $(1/2)^6 * (6/11) = 6/64 = 9.4\%$ , the return, in our simplified model, is 8% on the entire investment. This is approximately 200 basis points over Treasuries. If two or more drugs are successful, the structure caps the investment's return at



approximately 20%. The probability of this is  $100\% - 1.6\% - 9.4\% = 89\%$ . Hence, the weighted average return on the investment is  $1.6\%*0 + 9.4\%*8\% + 89\%*20\% = 18.5\%$ .

This example is obviously a simplification. Each of the drugs has a different probability of success, depending upon how far along each is in the approval process, and a different revenue profile. To reflect the different probabilities and different revenue streams, we developed a spreadsheet model that incorporates multiple drug compounds (and their specific probability of success, time to launch, and expected sales pattern) and a variable milestone/royalty structure. We then ran the spreadsheet model 500 times to provide us a range of outcomes as well as the expected results for returns and losses.

In our base case, we have made the following assumptions:

Product	Phase	JH Probability Of Approval	Launch	JH Peak Sales
BPH	Phase III	65%	2003	\$600 mm
Ketolide	Phase III	70%	2003	\$800 mm
Endothelin	Phase III	70%	2003	\$700 mm
CCM	Phase II	50%	2004	\$700 mm
Antimitotic	Phase I/II	40%	2004	\$500 mm
MMPI	Phase I	10%	2005	\$400 mm
FTI	PC	10%	2005	\$400 mm
Urokinase	PC	10%	2005	\$400 mm

... and calculated the average bond equivalent yield of this scenario to be approximately 17.3%. It is important to note that the expected IRRs are over a long period of time (15 years). Assuming that we could sell our future royalty stream after the fifth year, our five-year IRR would be about 22%.

#### Analysis of Return

The last step of our analysis was to determine what a fair economic return for this transaction should be. We have benchmarked this transactions in a number of ways, such as: R&D vehicles for pre-clinical compounds were sold with expected IRRs (over a three-to-five year period) of approximately 40%; Hambrecht & Quist has estimated pharmaceutical IRRs for single phase-II compounds to be 40% and single phase-III compounds to be 25%; the Palisade Partners (Sony movies) transaction that we participated in last year has an expected IRR of 20%; Elan Pharmaceuticals' pooled transaction has an expected five-year IRR of 13%; limited partner equity funds have about a 25% expected net IRR; and our proprietary analysis of the equity market's IRR for Abbott's entire R&D pipeline of 16-22%. Based on these comparisons, we think that an IRR of 17% over a long period of time is reasonable.

We also evaluated the relationship between our investment (and Abbott's) in the entire portfolio and the average royalty rate that we expect to receive – which is approximately 4-5%. We estimate that the current value of the compounds that Abbott is contributing to the transaction is about \$1 billion. During the four year investment period, Abbott expects to invest \$800 million on the compounds, in addition to our \$200 million. Based on these amounts, our investment is approximately 10% of the total invested dollars. Most pharmaceutical companies earn about a 50% pre-tax margin (excluding R&D expenses) on sales. On a net basis, then, our expected royalty and milestone percentage should be about 5%.

Risk Analysis.

The fundamental risks of this transaction are whether Abbott receives marketing approval from the FDA for a sufficient number of the Program Compounds and whether the commercial success of the Compounds are as we expect. In developing the expected return, we have made a number of reasonable assumptions regarding the probability of obtaining FDA approvals, acceptance of the products in the marketplace and competition. In many cases, our assumptions are significantly more conservative than Abbott's.

Again looking at our base case (which is demonstrated in the Chart I on the next page), the probability of no successful drugs is approximately 1.7% (the bar on the left). There are also a number of scenarios that produce a return of approximately 1% - 2%. These scenarios arise when only a cancer drug is successful. The cancer drugs have lower anticipated revenues, as well as lower probabilities of success, than any of the other drugs. This represents about 1.6% of the scenarios. All other scenarios give us a return of 9% or more. Assuming a 1-2% return represents a loss of half our original investment, the expected loss in this simulation is  $1.7\% + \frac{1}{2} \times 1.6\% = 2.5\%$ . Spread over a four year duration, the annual expected loss is 62 basis points which corresponds to the risk of a B1 rated bond.

We also ran a downside simulation, where the probabilities of success are discounted by 25% from the DiMasi study and the expected revenues are discounted by 25% from our base case (this is shown in Chart II on the next page).

The average return in this downside scenario is 9.3%. The probability that no drugs are successful rises dramatically to 4.9%. The low return scenario is now even lower (-2%) and also has a higher probability (2.7%). So, the annual expected loss is  $(4.9\% + .6 \times 2.7\%) / 4 = 165$  basis points which corresponds to the risk of a B1 rated bond.

CONFIDENTIAL  
JH 001216

CHART I  
BASE CASE

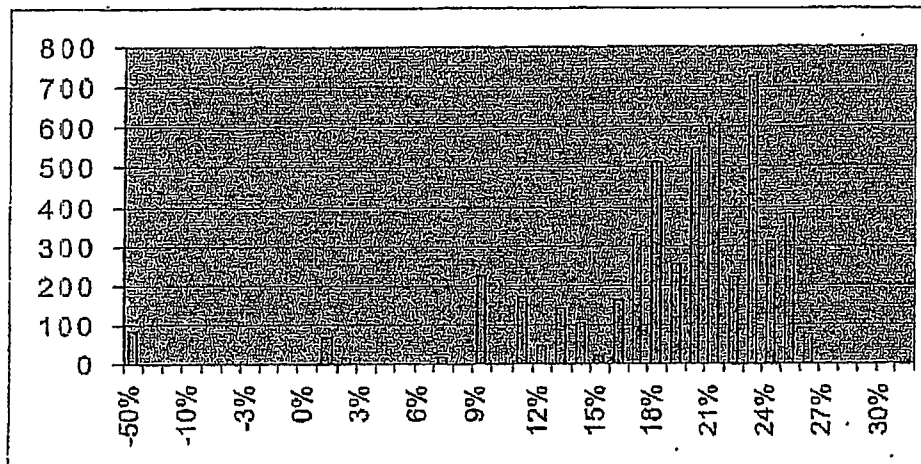
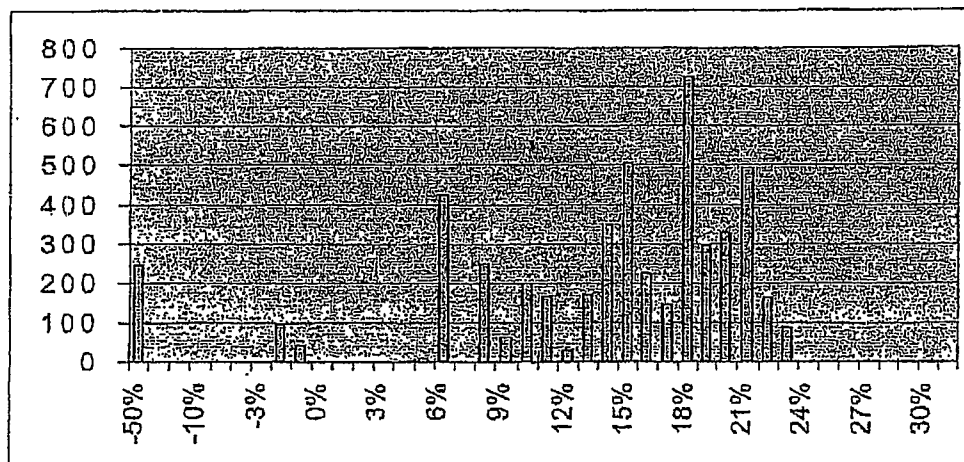


CHART II  
DOWNSIDE SCENARIO



## APPENDIX PRODUCT DESCRIPTIONS

### ABT-980

ABT-980 is a selective alpha blocker for the treatment of benign prostatic hyperplasia ("BPH"), a disorder that affects approximately 10 million middle-aged and elderly males in the U.S. The primary symptom of BPH is obstruction of urinary outflow and increased frequency of urination. Global sales of BPH products is approximately \$2 billion and is expected to continue to grow as the population ages and as better treatments become available. Currently, alpha blockers, including Abbott's Hytrin which recently became generic, are the most frequently prescribed pharmaceutical treatment for BPH. ABT-980 has the benefit of other alpha blockers, but since it only inhibits alpha receptors in the urinary tract, side effects on the cardiovascular system and central nervous system are expected to be reduced substantially.

One other selective alpha blocker, Boehringer Ingelheim's Flomax, the FDA and has been on the market since 1999. Flomax's current sales are approximately \$300 million. Abbott completed Phase II clinical trials and entered Phase III trials this past summer. In its Phase II trials, Abbott demonstrated that it is effectively equivalent (based on safety and efficacy) to Flomax.

This month, Abbott has learned that in long-term studies with rats, that about 15% of the rats given ABT-980 developed gallstones. Abbott does not know if these results are applicable to humans and at what frequency; however, there is no evidence of gallstones in humans to-date. In addition to its usual clinical trials, Abbott will try to determine whether gallstones will develop in humans over the long-term and what implications that may have. If ABT-980 fails due to this gallstone issue, Abbott will replace ABT-980 with another compound.

Abbott expects to submit ABT-980 for approval in June 2002 and launch the product in August 2003. The patent on ABT-980 expires in 2016.

### E-7010

E-7010 is a compound that Abbott licensed from Eisai Co. Ltd. in July 2000. E7010 has completed Phase I trials for various oncology applications. E7010 is an oral medication with a unique mechanism of action that enables it to stop cell mitosis with fewer side effects than current cytotoxic therapies. Although financial terms of the Abbott-Eisai agreement have not been publicly disclosed, Abbott is committing \$25 million in up-front and milestone payments to Eisai and will pay a double-digit royalty percentage on net sales. As a result of in-licensing E7010, Abbott has discontinued development of its own internally developed "anti-mitotic" compound.

Anti-mitotic compounds are not new. Taxol, the largest selling cancer drug, is an anti-mitotic. E7010, however, binds to a different site of a cell's microtubules than Taxol, and inhibits cell proliferation in a unique manner which is believed to cause fewer side effects.

E7010 has successfully completed Phase I clinical trials in Japan. These trials may be repeated in the U.S. but Abbott expects to move quickly into Phase II trials. Abbott expects to submit E7010 for approval in 2003 and launch the product in 2004. The patent on E7010 expires in 2011.

Our scientific consultants, Dr. Dennis A. Carson, UCSD School of Medicine, and Dr. John Kavanaugh, Jr., MD Anderson Cancer Center, did not have specific knowledge about the Abbott/Eisai compound. However, each researcher provided us with consistent critical benchmarks to evaluate the compound (such as whether the compound has been tested against specific cancer cell lines, whether the compound has been tested in combination with other anti-cancer agents. We have confirmed that Abbott independently addressed these critical benchmark and received positive results.

### ABT-773 (Ketolide)

ABT-773 is a member of a novel group of ketolide antibiotics within the macrolide group of antimicrobials. Ketolides have a similar mechanism of action to other macrolides such as Pfizer's *Zithromax* and Abbott's

*Biaxin*. Unlike macrolide antibiotics, ketolides are active against *s. pneumonia* and *h. influenza*. The antibiotics market size is approximately \$25 billion; macrolides account for approximately 13% and have an increasing market share. Only one ketolide (*Ketek*) is in advanced clinical trials; this compound, discovered by Aventis, was approved for sale in Europe and was been submitted to the FDA for approval in February 2000. Aventis expects to launch *Ketek* in 2001.

ABT-773 entered Phase III clinical trials this past summer. Abbott expects to submit ABT-773 for approval in June 2002 and launch the product in August 2003. The patent on ABT-773 expires in 2016.

Our scientific consultant, Dr. Robert C. Moellering, Jr., Harvard Medical School and Beth Israel Medical Center, confirmed the scientific rationale for ketolides and their market potential. Based on information that he has seen, Dr. Moellering believes that ABT-773 has more promise than Aventis' *Ketek*.

#### ABT-594

ABT-594 is a non-opioid, non-NSAID analgesic compound that is orally-administered for the treatment of diabetic neuropathic pain. In animal models, the compound has been shown to be substantially more potent than morphine with a better side effect profile. Neuropathic pain is a substantial and underserved market. Approximately 4-5 million people are thought to suffer from neuropathic pain but only a few medications provide complete pain relief and most medications have significant side effects. As more effective and tolerable medications become available, the neuropathic pain market is expected to experience significant growth.

ABT-594 is currently in Phase II clinical trials. If Phase II and Phase III trials are successful, Abbott expects to submit ABT-594 for approval in May 2003 and launch the product in July 2004. The patent on ABT-594 expires in 2016.

Our scientific consultant, Dr. Mitchell Max, NIH, eliminated an initial concern of ours that the "therapeutic window" of ABT-594 was too short and would potentially block approval. Dr. Max indicated that ABT-594's therapeutic window was acceptable. Dr. Max was not able to fully address toxicity issues raised by two of Abbott's competitors that the compound demonstrated opioid-like side effects in mice. These toxicity issues have not been found by Abbott in its mice or human trials. Dr. Max believed that ABT-594 showed a good profile in mice.

#### ABT-627

ABT-627 is an inhibitor of a family of endothelin peptides that cause constriction of vascular muscles and stimulate cell proliferation. ABT-627 is currently being developed by Abbott for the treatment of prostate cancer, and other cancer types.

Prostate cancer ("PCA") is the most common cancer to strike non-smoking men. Approximately 1.7 million men live with prostate cancer in the U.S., and there are approximately 180,000 newly diagnosed cases each year. The primary treatment of advanced stage PCA is hormone therapy. Patients receiving hormone therapy become resistant to this treatment after two to three years and then have a life expectancy of only about twelve months.

The primary benefit of ABT-627 is to reduce the pain associated with PCA and to delay the progression of the disease (but not necessarily improve survival).

ABT-627 is currently in Phase III clinical trials. If Phase III trials are successful, Abbott expects to submit ABT-627 for approval in December 2003 and launch the product in June 2004. The patent on ABT-627 expires in 2015.

Our scientific consultant, Dr. Joel Byron Nelson, MD, University of Pittsburgh, has indicated that ABT-627 is safe, significantly reduces pain associated with PCA, and delays disease progression.

**CONFIDENTIAL**  
JH 001219

#### MMPI

MMPI is an inhibitor of enzymes called matrix metalloproteinase that degrade a wide range of protein substrates. High expression of these enzymes occurs in cancer and is associated with the ability of tumors to grow, invade, develop new blood vessels and metastasize.

The MMPI field is competitive. More than 30 firms have filed patents and several companies have compounds in advanced clinical development. Abbott's MMPI has the potential competitive advantage of a better side effect profile. It appears to exhibit less arthritis and tendonitis of the upper joints than its competitors. This compound is currently being evaluated in Phase I clinical trials.

Abbott hopes to submit MMPI for approval in 2004 and launch the product in 2005. The patent on MMPI expires in 2018.

#### FTI

FTI is an inhibitor of enzymes called farnesyltransferase that assist certain proteins, such as the Ras protein, which are critical for malignant growths.

The FTI field is competitive. Approximately four compounds are in clinical development, and an additional five are in pre-clinical studies. Abbott has not yet chosen a specific FTI to enter into human clinical trials. It expects to enter human clinical trials in 2001.

Abbott hopes to submit FTI for approval in 2004 and launch the product in 2005. The patent on FTI is not expected to expire prior to 2014.

#### Urokinase

Urokinase is an inhibitor of enzymes called urokinase which are believed to promote the metastases of tumors by breaking down cell membranes.

The Urokinase field is less well-developed than MMPI and FTI. No compound has currently made it into clinical trials. Abbott is currently evaluating several compounds. If Abbott fails to take a Urokinase compound into clinical trials, Abbott will substitute another Phase I compound into the Program.

Abbott hopes to submit Urokinase for approval in 2004 and launch the product in 2005. The patent on Urokinase is not expected to expire prior to 2014.

Our scientific consultant, Dr. Edward Sausville, National Cancer Institute, has indicated that "cytostatic" therapies such as MMPI, FTI and Urokinase may be useful upon recurrence of cancer as a means to stopping the progression of the disease. He believes that they will be useful in combination with other therapies and may not be exceptional compounds by themselves.

CONFIDENTIAL  
JH 001220

**PLs' LG**



John Hancock Life Insurance Company  
Boston, Massachusetts

*Committee of Finance Records*

October 10, 2000

A meeting of the Committee of Finance was held on this date, with Chairman Brown presiding.

Present: Messrs. Brown, D'Alessandro, Aborn, Gifford, Linde, Morton,  
Syron and Tarr

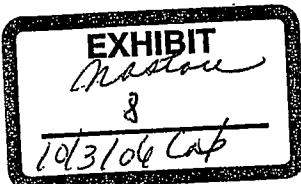
Also Present: Messrs. DeCiccio, Budd and Rubenstein, Secretary

REDACTED

The meeting was called to order by Chairman Brown. The minutes of the prior meeting were approved.

REDACTED

The Bond and Corporate Finance Group materials were presented by Roger Nastou. A question and answer period followed the presentation. See Attachment B for Votes approving investments with respect to Abbott Laboratories and and Reports of Purchases, Sales, Modifications and Swaps approved between meetings. A Report of Bond and Corporate Finance Group Investments and Available Capacity in Below AA - Country Investments was submitted. Materials are on file with the Secretary.



Numerous transaction reports were submitted by the Company's investment managers. These are included in the minutes.

CONFIDENTIAL  
JH 005551



Meeting of October 10, 2000

John Hancock Life Insurance Company  
Committee of Finance Records

Page 4

Attachment B

VOTED:

\$ 99,000,000.  
\$ 110,000,000.

To authorize purchase, at par, of up to

for the General Account, and up to  
for the Guaranteed Benefit Sub Account.

**ABBOTT LABORATORIES**

\$220 Million Research and Development Funding Commitment

Subject to approval of all legal  
details by our Law Department.

**REDACTED**

**CONFIDENTIAL**  
JH 005552

Meeting of October 10, 2000

John Hancock Life Insurance Company  
Committee of Finance Records

Page 328

There being no further business, the meeting was adjourned.

ATTEST:



SECRETARY

Also Attending:

Messrs./Mss. Acford, Agretelis, Atamian, Blewitt, Britt, Budde, Clark, Curtis, Davis, Della Piana, Felton, Freiburger, Garrison, Gottlieb, Haahsy, Han, Harris, Hartz, Henderson, Hines, Johnson, J., Lacasse, McAneny, McDonough, J., McDonough, K., McPadden, Mongeau, Nagle, Nastou, Navin, Nectow, Nierintz, Panthaki, Ray, Reitano, Revers, Santosuosso, Schaeffer, Stapleton, Steggall, Talbot, White, Wise and Yang.

CONFIDENTIAL  
JH 005553

**PLs' LI**

Research Funding Agreement

Page 1 of 1

---

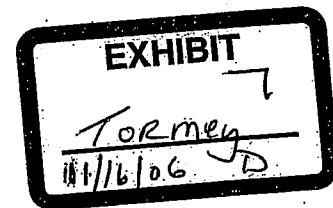
**From:** Daphne Pals [daphne.pals@abbott.com]  
**Sent:** Tuesday, October 17, 2000 6:59 PM  
**To:** Lee, Brewster; Blewitt, Stephen  
**Cc:** Brian Smith; Philip Deemer  
**Subject:** Research Funding Agreement

Brian Smith has asked me to help complete this Agreement. Attached for your review and comment is a red-lined and clean copy of the revised Research Funding Agreement.

As I will be out of the office tomorrow, if you have any difficulties opening the documents, please contact my assistant, Bill Adams, at 847-935-5747.

I look forward to talking to you on Thursday.

Daphne Pals  
847-937-6481



CONFIDENTIAL  
JH 004385

Abbott Draft 10/17/00

RESEARCH FUNDING AGREEMENT

by and between

ABBOTT LABORATORIES

and

JOHN HANCOCK LIFE INSURANCE COMPANY

dated as of

October \_\_, 2000

CONFIDENTIAL  
JH 004386

## TABLE OF CONTENTS

<b>ARTICLE I - DEFINITIONS</b>	<b>1</b>
<b>ARTICLE 2 - ANNUAL RESEARCH PROGRAM</b>	<b>7</b>
2.1 <u>PROGRAM TERM</u>	7
2.2 <u>RESEARCH PLAN</u>	7
2.3 <u>CONDUCT OF RESEARCH</u>	8
2.4 <u>SUBCONTRACTING RESEARCH</u>	8
2.5 <u>RESEARCH REPORTS AND RECORDS</u>	8
<b>ARTICLE 3 - RESEARCH FUNDING</b>	<b>9</b>
3.1 <u>JOHN HANCOCK PROGRAM PAYMENTS</u>	9
3.2 <u>ABBOTT PROGRAM PAYMENTS</u>	9
3.3 <u>CARRYOVER PROVISIONS</u>	9
3.4 <u>TERMINATION OF JOHN HANCOCK'S PROGRAM PAYMENT OBLIGATION</u>	10
3.5 <u>HANCOCK FUNDING OBLIGATION</u>	10
<b>ARTICLE 4 - PRODUCT RESEARCH AND DEVELOPMENT</b>	<b>10</b>
4.1 <u>COMMERCIALLY REASONABLE EFFORTS</u>	10
4.2 <u>MARKETING AND SALE RESPONSIBILITY</u>	11
4.3 <u>FAILURE OF PROGRAM COMPOUND TO PROGRESS</u>	11
4.4 <u>COMPOUND ABT-627</u>	11
4.5 <u>ARM'S-LENGTH</u>	12
<b>ARTICLE 5 - PROGRAM INVENTIONS</b>	<b>12</b>
5.1 <u>OWNERSHIP</u>	12
5.2 <u>PATENT PROSECUTION AND MAINTENANCE</u>	12
5.3 <u>ENFORCEMENT</u>	12
<b>ARTICLE 6 - MILESTONE PAYMENTS TO JOHN HANCOCK</b>	<b>12</b>
6.1 <u>CLOSING FEE</u>	12
6.2 <u>MANAGEMENT FEE</u>	13
6.3 <u>MILESTONE NOTIFICATION AND PAYMENTS</u>	13
<b>ARTICLE 7 - ROYALTIES</b>	<b>14</b>
7.1 <u>ROYALTY RATES</u>	14
7.2 <u>ROYALTY TERM</u>	14
<b>ARTICLE 8 - ROYALTY REPORTS AND ACCOUNTING</b>	<b>14</b>
8.1 <u>REPORTS, EXCHANGE RATES</u>	14
8.2 <u>AUDITS</u>	15
8.3 <u>CONFIDENTIAL FINANCIAL INFORMATION</u>	16
8.4 <u>ACCOUNTING PRINCIPLES</u>	16
<b>ARTICLE 9 - PAYMENTS</b>	<b>16</b>
9.1 <u>PAYMENT TERMS</u>	16
9.2 <u>PAYMENT METHOD</u>	16
9.3 <u>WITHHOLDING TAXES</u>	16
9.4 <u>LATE PAYMENTS</u>	17

**CONFIDENTIAL**  
JH 004387

-ii-

<b>ARTICLE 10 - CONFIDENTIALITY</b>	<b>17</b>
10.1 <u>NONDISCLOSURE OBLIGATIONS</u>	17
10.2 <u>PERMITTED DISCLOSURES</u>	17
10.3 <u>PUBLICITY REVIEW</u>	17
<b>ARTICLE 11- TERM AND TERMINATION</b>	<b>18</b>
11.1 <u>EXPIRATION</u>	18
11.2 <u>MATERIAL BREACH</u>	18
11.3 <u>EFFECT OF EXPIRATION OF TERMINATION</u>	18
<b>ARTICLE 12 - WARRANTIES AND INDEMNITY</b>	<b>18</b>
12.1 <u>JOHN HANCOCK REPRESENTATIONS AND WARRANTIES</u>	18
12.2 <u>ABBOTT REPRESENTATIONS AND WARRANTIES</u>	19
12.3 <u>NO CONFLICT</u>	22
12.4 <u>COMPLIANCE WITH LAW</u>	22
12.5 <u>CERTAIN BREACHES</u>	22
12.6 <u>INDEMNIFICATION OF JOHN HANCOCK</u>	22
12.7 <u>PROCEDURE</u>	22
12.8 <u>INSURANCE</u>	23
12.9 <u>SURVIVAL</u>	23
<b>ARTICLE 13 - FORCE MAJEURE</b>	<b>23</b>
<b>ARTICLE 14 - ASSIGNMENT</b>	<b>23</b>
<b>ARTICLE 15 - SEVERABILITY</b>	<b>24</b>
<b>ARTICLE 16 - MISCELLANEOUS</b>	<b>24</b>
16.1 <u>NOTICES</u>	24
16.2 <u>APPLICABLE LAW</u>	25
16.3 <u>ENTIRE AGREEMENT</u>	25
16.4 <u>HEADINGS</u>	25
16.5 <u>INDEPENDENT CONTRACTORS</u>	25
16.6 <u>PERFORMANCE BY AFFILIATES</u>	26
16.7 <u>ALTERNATIVE DISPUTE RESOLUTION</u>	26
16.8 <u>WAIVER</u>	26
16.9 <u>COUNTERPARTS</u>	26

EXHIBIT 1.:	Annual Research Plan - First Program Year
EXHIBIT 1.:	List of Program Compounds
EXHIBIT 6.:	Program Compound Status
EXHIBIT 9.2:	Wiring Instructions for John Hancock
EXHIBIT 12.2(d):	Program Compound Detail
EXHIBIT 12.2(e):	Patents, etc.
EXHIBIT 16.7:	Alternative Dispute Resolution

**CONFIDENTIAL**  
**JH 004388**

Abbott Draft 10/17/00

RESEARCH FUNDING AGREEMENT

This Research Funding Agreement is made as of \_\_\_\_\_, 2000, by and between Abbott Laboratories, an Illinois corporation ("Abbott"), with its principal offices at 100 Abbott Park Road, Abbott Park, Illinois 60064-6049, and John Hancock Life Insurance Company, a Massachusetts corporation ("John Hancock"), with its principal offices at 200 Clarendon Street, Boston, Massachusetts 02117.

WITNESSETH

WHEREAS, Abbott is a global healthcare company actively engaged in the research and development of human pharmaceutical products;

WHEREAS, Abbott is interested in obtaining additional funding to support such research and development activities with respect to certain pharmaceutical products which are under development; and

WHEREAS, John Hancock is interested in providing such additional funding in exchange for the right to receive future milestone and royalty payments from Abbott.

NOW, THEREFORE, in consideration of the foregoing and the mutual covenants and undertakings contained herein, the parties hereto agree as follows:

ARTICLE I  
DEFINITIONS

In addition to the other terms defined elsewhere herein, the following terms shall have the following meanings when used in this Agreement (and any term defined in the singular shall have the same meaning when used in the plural and vice versa, unless stated otherwise):

1.1 "ABT-627" shall have the meaning given in Section 1.32.

1.2 "Affiliate" shall mean, with respect to each party, any corporation or other form of business organization, which directly or indirectly owns, controls, is controlled by, or is under common control with, such party. An entity shall be regarded as being in control of another entity if the former entity has the direct or indirect power to order or cause the direction of the policies of the other entity whether (i) through the ownership of fifty percent (50%) or more in the United States, or thirty percent (30%) or more outside the United States, of the outstanding voting securities (or other ownership interest for a business organization other than a corporation) of that entity; or (ii) by contract, statute, regulation or otherwise.

1.3 "Aggregate Carryover Amount" shall have the meaning given in Section 3.3.

CONFIDENTIAL  
JH 004389



-2-

1.4 "Aggregate Spending Target" shall mean Six Hundred Twenty Million Dollars (\$620,000,000), such amount being the sum of the aggregate Program Payments to be made by John Hancock pursuant to Section 3.1 and the aggregate expenditures to be made by Abbott pursuant to Section 3.2.

1.5 "Annual Carryover Amount" shall have the meaning given in Section 3.3.

1.6 "Annual Minimum Spending Target" for each Program Year shall mean the sum of (i) the Program Payment of John Hancock for such Program Year as specified in Section 3.1 (without giving effect to any deferral or other change under Section 3.3), (ii) Fifty Million Dollars (\$50,000,000), and (iii) any Annual Carryover Amount for such Program Year pursuant to Section 3.3.

1.7 "Annual Research Plan" shall mean a reasonably and consistently detailed statement of Abbott's objectives, activities, timetable and budget for its research and development activities related to the Program Compounds for every Program Year remaining in the Program Term. The Annual Research Plan for the first Program Year is attached as Exhibit 1.

1.8 "Bundled Product" shall have the meaning given in paragraph (b) of the definition of Net Sales.

1.9 "Combination Product" shall mean any product containing one or more Program Compounds combined as a single pharmaceutical product with one or more other therapeutically active ingredients.

1.10 "Commercially Reasonable Efforts" [subject to discussion] shall mean efforts which are consistent with those normally used by other pharmaceutical companies with respect to other pharmaceutical products which are of comparable [potential] commercial value and market potential at a similar stage of development or product life, taking into account, without limitation, issues of safety and efficacy, product profile, proprietary status, the regulatory environment and the status of the product and other relevant scientific factors.

1.11 "Confidential Information" shall have the meaning given in Section 10.2.

1.12 "Delivery System Product" shall have the meaning given in the definition of Net Sales.

1.13 "Dollars" or "\$" means United States dollars.

1.14 "Eisai Agreement" shall mean the [agreement] dated June 29, 2000 between Eisai Co. Ltd. and Abbott related to the Program Compound "E7010".

1.15 "Execution Date" shall mean the date set forth in the introductory paragraph to this Agreement.

CONFIDENTIAL  
JH 004390

-3-

1.16 "FDA" shall mean the U.S. Food and Drug Administration or any successor entity thereto.

1.17 "First Commercial Sale" shall mean the first sale of a Product in a given country by Abbott, its Affiliates or Licensees to an unrelated third person after Regulatory Approval has been granted in such country.

1.18 "Intellectual Property" shall have the meaning given in Section 12.2.

1.19 "International Territory" shall mean all areas of the world outside the U.S. Territory (including Puerto Rico and the U.S. Virgin Islands).

1.20 "Investigational New Drug Application" shall have the meaning given in Section 6.3.

1.21 "Licensee" shall mean any party directly licensed by Abbott or its Affiliates to distribute or sell Products pursuant to a written license agreement on arm's-length terms and conditions.

1.22 "Losses" shall mean any claims, demands, liabilities, costs, damages, judgments, settlements and other reasonable expenses (including attorneys' fees).

1.23 "NDA" shall mean a New Drug Application filed with the FDA for the purpose of obtaining Regulatory Approval of a Product in the U.S. Territory.

1.24 "Net Sales" shall mean:

- (a) the total gross sales of the Products (or, for purposes of clauses (b) and (c), the Bundled Products and Combination Products), in each case as set forth on the invoices for such sales by Abbott, its Affiliates and Licensees to unaffiliated third parties in any given period, plus, if applicable, the fair market value of all properties and services received in consideration of a sale of Products, Bundled Products or Combination Products, as applicable, by Abbott, its Affiliates and Licensees to unaffiliated third parties during such period, less the following deductions directly paid or actually incurred by Abbott, its Affiliates or Licensees during such period with respect to the sale of the Products, Bundled Products or Combination Products, as applicable, to the extent included in the gross invoiced sales price therefor:
  - (i) discounts, credits, rebates, allowances, adjustments, rejections, recalls and returns;
  - (ii) price reductions or rebates, retroactive or otherwise, imposed by government authorities;

CONFIDENTIAL  
JH 004391

- (iii) sales, excise, turnover, inventory, value-added and similar taxes assessed on the royalty-bearing sale of Products;
  - (iv) transportation, importation, insurance and other handling expenses directly chargeable to the royalty-bearing sale of Products;
  - (v) charge backs granted to unaffiliated drug wholesalers; and
  - (vi) the portion of management fees paid to unaffiliated group purchasing organizations that relate specifically to the royalty-bearing sale of Products.
- (b) With respect to a Product which is sold together with any other products and/or services in a country at a unit price, whether packaged together or separately (a "Bundled Product"), the Net Sales of such Bundled Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Bundled Product shall be determined on a country-by-country basis as follows:
- (i) multiply the Net Sales of such Bundled Product in such country by the fraction  $A/(A+B)$  where A is the average selling price of such Product in such country when sold separately and B is the total of the average selling prices in such country of each such other product(s) and/or service(s) in such Bundled Product when sold separately; or
  - (ii) if (x) either the average selling price of such Product or the total of the average selling prices of each such other products and/or services in such Bundled Product in such country is not available as of such date or (y) such Product is not sold separately in such country, multiply the Net Sales of such Bundled Product in such country by a percentage determined by the mutual agreement of the Parties which represents the proportionate economic value in such country of such Product relative to the economic value in such country contributed by the other products and/or services in such Bundled Product.
- (c) With respect to a Combination Product, the Net Sales of such Combination Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Combination Product shall be determined on a country-by-country basis as follows:
- (i) multiply the Net Sales of such Combination Product in such country by the fraction  $A/(A+B)$ , where A is the total of the average selling prices of the Program Compounds in such Combination Product, when sold separately in such country and B

-5-

is the total of the average selling prices of each other therapeutically active ingredient when sold alone as a pharmaceutical product in such country; or

- (ii) if (x) either the average selling price of all Program Compounds in such Combination Product or the total of the average selling prices of each other therapeutically active ingredient in such Combination Product in such country is not available or (y) such Program Compounds are not sold separately in such country, multiply the Net Sales of such Combination Product by a percentage determined by mutual agreement of the Parties, which represents the proportionate economic value in such country of all Program Compounds in such Combination Product relative to the economic value in such country contributed by all other therapeutically active ingredients in such Combination Product.
- (d) For purposes of this paragraph (d), a "Premium Delivery System" means any delivery system comprising device(s), equipment, instrumentation or other components (but not solely containers or packaging) designed to assist in the administration of a Product[, such as the Abbott ADD-Vantage® System]. With respect to a Product which is sold together with a Premium Delivery System (a "Delivery System Product") in a country at a unit price, the Net Sales of such Delivery System Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Product shall be determined on a country-by-country basis as follows:
- (i) if the Product is sold separately without the Premium Delivery System in a country, reduce the Net Sales of such Delivery System Product in such country by the amount that the average selling price of the Delivery System Product in such country exceeds the average selling price of such Product as sold separately in such country; or
  - (ii) if the Product is not sold separately without the Premium Delivery System in such country, reduce Net Sales of such Delivery System Product by an amount, determined by mutual agreement of the Parties, which represents the proportionate economic value in such country added by the Premium Delivery System.
- (e) With respect to Compound ABT-627 [define], if Compound ABT-627 is developed and marketed by Abbott for one or more cancer indications and one or more non-cancer indications, Net Sales shall be based upon sales of Product only for the cancer indication(s). If the Product is sold with different dosage strengths for the cancer indications and non-cancer indications, Net Sales shall be calculated based on the sales of the dosage strength(s) which are approved by the FDA for the treatment of cancer. If

CONFIDENTIAL  
JH 004393

-6-

any dosage strength is the same for one or more cancer indications and one or more non-cancer indications, the Parties shall mutually agree to a formula, based upon IMS [define] or other market research data, that allocates the sales of such dosage strength between the cancer indication(s), which would be included as part of Net Sales, and the non-cancer indication(s) which would be excluded from Net Sales.

1.25 "Neutral" shall have the meaning given in Exhibit 16.7.

1.26 "Parties" shall mean Abbott and John Hancock.

1.27 "Phase I Clinical Trial" shall mean those clinical trials which utilize a limited number of human beings to preliminarily address safety and to determine what doses can be safely tolerated.

1.28 "Phase II Clinical Trial" shall mean those controlled clinical trials, the primary objective of which is to ascertain additional data regarding the safety and tolerance of one of the Program Compounds and preliminary data regarding such Program Compound's efficacy.

1.29 "Phase III Clinical Trial" shall mean one or a series of controlled pivotal studies of a specific Product by administration of such Product to human beings where the principal purpose of such trial is to provide confirmatory safety and efficacy data necessary to support the filing for Regulatory Approval of a Product.

1.30 "Premium Delivery System" shall have the meaning given in paragraph (d) of the definition of Net Sales.

1.31 "Product" shall mean any product containing one or more of the Program Compounds as an active ingredient, alone or in combination with other active ingredients (including any Bundled Product and any Combination Product).

1.32 "Program Compounds" shall mean the preclinical, Phase I, Phase II, and Phase III compounds listed on Exhibit 1.32, as well as any back-up compounds added by Section 4.3, and any line extensions, any new formulations, all indications and any improvements, derivatives and modifications thereof; provided, however, that with respect to Compound ABT-627 (hereinafter, "Compound ABT-627"), it shall only be considered a Program Compound to the extent that it is used to treat cancer.

1.33 "Program Inventions" shall have the meaning given in Section 5.1.

1.34 "Program Payments" shall have the meaning given in Section 3.1.

1.35 "Program Related Costs" shall mean (i) all direct and indirect costs and expenses that are incurred by Abbott on the Research Program during a given Program Year; (ii) any payments made by Abbott to John Hancock pursuant to Sections 6.1, 6.2 and 6.3(a) through (e); and (iii) the milestone and license fees paid by Abbott to Eisai Co. Ltd. with respect to the Program Compound "E7010" pursuant to the Eisai Agreement. In no event shall any payments

**CONFIDENTIAL**  
**JH 004394**

-7-

made by Abbott to John Hancock pursuant to Section 6.3(f) constitute Program Related Costs. Exhibit 1.35 is an example of Program Related Costs for a Program Compound.

1.36 "Program Term" shall mean a period of four (4) consecutive Program Years.

1.37 "Program Year" shall mean a period of twelve (12) consecutive calendar months, with the first Program Year commencing on \_\_\_\_\_, 2000 and each subsequent Program Year commencing on the anniversary of such date.

1.38 "Quarterly Reporting Period" shall mean the calendar quarter with respect to the U.S. Territory and a fiscal quarter ending on the final day of February, May, August and November (as the case may be) for the International Territory; provided, however, that if Abbott adopts the calendar year as its fiscal year for the International Territory, then the Quarterly Reporting Period for the International Territory shall also be the calendar quarter.

1.39 "Research Program" shall mean all of Abbott's, its Affiliates and Subcontractors' activities directed towards obtaining Regulatory Approval for the Products, including research, development, safety and efficacy studies, clinical trials, process development, formulation work, regulatory, quality, data collection and analysis and project management.

1.40 "Regulatory Approval" shall mean: (i) with respect to the U.S. Territory, the receipt of approval from the FDA to market a Product in the U.S. Territory; and (ii) with respect to any country in the International Territory, receipt of the governmental approvals required to market a Product in such country, including any pricing and reimbursement authorization required in such country.

1.41 "Royalty Term" shall mean, with respect to each Product in each country, a period of ten (10) years from the date of First Commercial Sale of such Product in such country.

1.42 "Subcontractor" shall have the meaning given in Section 2.4.

1.43 "Territory" shall mean both the U.S. Territory and the International Territory.

1.44 "U.S. Territory" shall mean the United States of America, excluding Puerto Rico and the U.S. Virgin Islands.

## ARTICLE 2 ANNUAL RESEARCH PROGRAM

2.1 Program Term. The Research Program shall be conducted by Abbott during the Program Term, and beyond the Program Term until Abbott either abandons development in accordance with the terms hereof or receives Regulatory Approval for each Program Compound.

2.2 Research Plan. The Research Program shall be conducted by Abbott in each Program Year in accordance with the Annual Research Plan for such Program Year. The Annual Research Plan will be provided to John Hancock until Abbott either abandons development in

CONFIDENTIAL  
JH 004395



-8-

accordance with the terms hereof or receives Regulatory Approval for each Program Compound in the U.S. Territory. The Annual Research Plan shall be prepared by Abbott and presented to John Hancock at least sixty (60) days prior to the start of each Program Year. The Annual Research Plan for the first Program Year is attached as Exhibit 1. Abbott may modify the Annual Research Plan from time to time in order to best meet the objectives of the Research Program. Any such modifications to the Annual Research Plan shall be promptly provided to John Hancock.

2.3 Conduct of Research. Abbott shall use Commercially Reasonable Efforts to conduct the Research Program in good scientific manner and using good laboratory practices, to achieve the objectives of the Research Program efficiently and expeditiously and to comply with all applicable laws and regulations. Notwithstanding anything in this Agreement to the contrary, Abbott does not represent, warrant or guarantee that the Research Program will be successful in whole or in part or result in the registration or commercialization of any pharmaceutical products or that any Products obtaining Regulatory Approval will be a commercial success.

2.4 Subcontracting Research. Abbott may subcontract or outsource to Affiliates or third persons (each, a "Subcontractor") any portion of the Annual Research Plan. Each non-affiliated Subcontractor shall enter into a confidentiality agreement with Abbott and agreements acknowledging Abbott's exclusive ownership of the Program Compounds and shall comply with the terms hereof and with all applicable laws and regulations, including good laboratory practices, with respect to its work on the Research Program. Abbott shall supervise and be responsible under this Agreement for the work of such Subcontractor on the Research Program and no subcontracting or outsourcing shall relieve Abbott of any of its obligations hereunder.

2.5 Research Reports and Records. Abbott shall on an annual basis [no later than the last day of each Program Year] [This report must be provided before John Hancock can be obligated under section 3 to make a subsequent Program Payment], provide John Hancock with a reasonably detailed report setting forth the status of the Research Program and all Program Related Costs expended by Abbott during such Program Year. Such report shall also contain such other information related thereto as John Hancock may reasonably request from time to time. Abbott shall, and shall cause each Subcontractor to, maintain complete and accurate records, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes and for purposes of demonstrating compliance with the terms hereof, that fully and properly reflect all work done, results achieved and Program Related Costs expended in performance of the Research Program. The books and records of Abbott and each Subcontractor related to the Research Program, including, without limitation, those related to the expenditure of Program Related Costs, shall be subject to copying, inspection and audit by (and at the expense of) John Hancock at any time and from time to time. Such audit shall occur upon reasonable notice and during normal business hours by an independent auditor selected by John Hancock and reasonably acceptable to Abbott. John Hancock and its independent auditor shall maintain such records and information of Abbott in confidence in accordance with Article 10 and shall not use such records or information except to the extent permitted by this Agreement, including any enforcement of the provisions hereof. In the event that such audit reveals any material breach of Abbott's responsibilities hereunder, Abbott shall (i) pay the reasonable fees and expenses charged by such auditor, and (ii) fully and promptly cure such breach.

CONFIDENTIAL  
JH 004396

**ARTICLE 3**  
**RESEARCH FUNDING**

3.1 **John Hancock Program Payments.** John Hancock shall make the following installment payments for the applicable Program Year to Abbott to help support the Research Program (the "Program Payments"):

<u>Payment Date</u>	<u>Payment Amount</u>	<u>Program Year</u>
Execution Date	\$50,000,000	first
First Anniversary of Execution Date	\$55,000,000	second
Second Anniversary of Execution Date	\$55,000,000	third
Third Anniversary of Execution Date	\$60,000,000	fourth

Such funds shall be expended by Abbott on Program Related Costs and for no other purpose.

3.2 **Abbott Program Payments.** Abbott shall spend on Program Related Costs: (i) during each Program Year, at least the Annual Minimum Spending Target for such Program Year and (ii) at least the Aggregate Minimum Spending Target during the Program Term. John Hancock's sole and exclusive remedies for Abbott's failure to fund the Research Program in accordance with this Section 3.2 (but not for any other breach of Abbott's other obligations) are set forth in Sections 3.3 and 3.4.

3.3 **Carryover Provisions.** Abbott shall be permitted to change its funding obligations under Section 3.2 only as follows:

- (i) If in any Program Year Abbott spends on Program Related Costs, the full amount of the Program Payment provided by John Hancock for such Program Year, but does not spend the full amount of the Annual Minimum Spending Target for such Program Year (including any Annual Carryover Amounts from any prior Program Years), Abbott will spend the difference between its expenditure on Program Related Costs for such Program Year and the Annual Minimum Spending Target for such Program Year (the "Annual Carryover Amount") in the subsequent Program Year. John Hancock's obligation to make any Program Payment for such subsequent Program Year, if any, pursuant to Section 3.1, shall be deferred until the time that Abbott notifies John Hancock that it has spent the Annual Carryover Amount in such subsequent Program Year, and
- (ii) If for each Program Year Abbott spends on Program Related Costs at least the Annual Minimum Spending Target, with or without utilizing the carryover permitted in paragraph (i), but does not expend the full amount of the Aggregate Spending Target during the Program Term, Abbott will expend the difference between its expenditures for Program Related Costs during the Program Term and the Aggregate Spending Target (the

**CONFIDENTIAL**  
**JH 004397**



-10-

"Aggregate Carryover Amount") on Program Related Costs during the subsequent fiscal year commencing immediately after the end of the Program Term. If Abbott does not spend the Aggregate Carryover Amount on Program Related Costs during such subsequent fiscal year, Abbott will refund to John Hancock one-third of the Aggregate Carryover Amount that remains unspent by Abbott, within thirty (30) days of the end of such subsequent fiscal year.

3.4 Termination of John Hancock's Program Payment Obligation. If Abbott: (i) abandons development of all Program Compounds during the Program Term; (ii) does not expend during any Program Year the full amount of the Program Payment made by John Hancock for such Program Year; (iii) does not reasonably demonstrate in its Annual Research Plan, its intent and reasonable expectation to expend Program Related Costs during the next Program Year in excess of the Program Payment provided by John Hancock for such year; or (iv) does not reasonably demonstrate, in its Annual Research Plan, its intent and reasonable expectation to expend Program Related Costs during the Research Term in excess of the Aggregate Spending Target, John Hancock's obligation to make any remaining Program Payments pursuant to Section 3.1 shall cease. In addition, in the case of either (i) or (ii) above, Abbott shall refund (not later than the 10th day following such event) to John Hancock the amount, if any, by which the Program Payment made by John Hancock for such year, if any, exceeds one-half of the Program Related Costs actually spent by Abbott during that Program Year.

3.5 Hancock Funding Obligation. John Hancock's entire obligation hereunder shall be limited to providing the Program Payments set forth in Section 3.1. Abbott shall be solely responsible for funding all Program Related Costs in excess of the Program Payments from John Hancock.

#### ARTICLE 4 PRODUCT RESEARCH AND DEVELOPMENT

4.1 Commercially Reasonable Efforts. Abbott shall be solely responsible for the clinical development, government approval, manufacturing, marketing, sales and distribution of Products. Abbott will use, and will cause each of its Affiliates and Licensees to use, Commercially Reasonable Efforts to pursue the clinical development, government approval, manufacturing, marketing, sales and distribution of Products throughout the Territory. The obligations of Abbott, its Affiliates and Licensees with respect to any Product under this Article 4 are expressly conditioned upon the safety, efficacy and commercial feasibility of each Product, but no license, assignment or other transfer of rights by Abbott (by operation of Article 14 or otherwise) will modify or reduce Abbott's obligations hereunder. [It is the parties' expectation that under normal circumstances][addressed by proviso at end of sentence?] Abbott will file for Regulatory Approval with respect to each Product in Europe within two (2) years from the date of the NDA filing for such Product in the U.S. Territory and in Japan within five (5) years from such NDA filing date; provided, however, that these time frames may be extended or otherwise altered based upon unforeseen circumstances that legitimately impact such regulatory filings in such foreign jurisdictions.

CONFIDENTIAL  
JH 004398

-11-

4.2 Marketing and Sale Responsibility: Without limiting the generality of Section 4.1, within six (6) months of obtaining Regulatory Approval for a Product in a given country, Abbott, its Affiliates or Licensees shall commence to market and sell such Product in such country. Abbott's obligation to market and sell a Product shall not apply [Why doesn't "Commercially Reasonable Efforts" address all of this?] to a Product in any country if Abbott has not commenced or has ceased marketing and selling such Product in such country substantially/primarily on account of adverse business or financial conditions caused by the regulatory authorities or other governmental authorities of such country (including not commencing marketing and selling in a country where the regulatory authorities have price or reimbursement approval and the price or reimbursement approval [or that proposed by the regulatory authorities or government authorities] is unacceptable to Abbott) which causes the marketing and sale of such Product in such country to be contrary to the financial best interests of John Hancock and Abbott; provided, however, that Abbott, its Affiliates or Licensees shall commence or resume marketing and sale of such Product in such country as soon as reasonably practical after such adverse business or financial conditions cease to exist.

4.3 Failure of Program Compound to Progress: If a Program Compound fails to progress past Phase I Clinical Trial (i.e., does not enter a Phase II Clinical Trial) (a "Failed Program Compound"), and Abbott initiates the development of a back-up compound, including any in-licensed back-up compound in the same class of compounds with the same mechanism of action for the same indications as the Failed Program Compound, during the Program Term or any period immediately thereafter during which the Aggregate Carryover Amount is being spent, then such back-up compound shall be deemed a Program Compound. With respect to any Failed Program Compound for which Abbott does not initiate development of a back-up compound as set forth above, then Abbott shall have no further obligations to John Hancock with respect to such Failed Program Compound. With respect to any Program Compound which enters a Phase II Clinical Trial but which Abbott thereafter ceases the development of, John Hancock shall have no further rights with respect to such Program Compound or any other back-up compound or in-licensed back-up compound developed by Abbott.

4.4. Compound ABT-627. With respect to Compound ABT-627, if Abbott, its Affiliates or Subcontractors initiates a Phase [II] Clinical Trial for one or more non-cancer indications during the Program Term or any period immediately thereafter during which the Aggregate Carryover Amount is being spent, Abbott will provide notice thereof to John Hancock together with information similar to that which John Hancock received in connection with the Program Compounds hereunder. Abbott will provide additional information concerning Compound ABT-627 and such trial as reasonably requested by John Hancock. Abbott agrees to give John Hancock the option, exercisable in John Hancock's sole discretion, to provide approximately 33 1/3% of the additional research funding required with respect to Compound ABT-627 for all non-cancer indications. John Hancock shall have forty-five (45) days from Abbott's notice to notify Abbott of its interest. If John Hancock has not notified Abbott within such forty-five (45) day period, the option shall be deemed expired. If John Hancock participates in such funding, Net Sales of Products shall include Net Sales generated by sales of Compound ABT-627 for such additional indication(s) upon Abbott's receipt of FDA approval for such indication(s).

CONFIDENTIAL  
JH 004399

-12-

4.5. Arm's-Length. Abbott shall not research, develop, manufacture, market, sell, distribute, out-license or otherwise treat any Program Compounds or Products differently, as compared to any other Abbott compounds or products, on account of any of John Hancock's rights hereunder. Furthermore, all distribution agreements, licenses, out-licenses and other agreements relating to the research, development, manufacturing, marketing, sale, distribution, licensing, out-licensing or divestiture of and all other transactions involving any Program Compounds or Products to or with any third party (except to Abbott's Affiliates) shall be on arm's-length terms and conditions.

## ARTICLE 5 PROGRAM INVENTIONS

5.1 Ownership. All inventions, innovations, ideas, discoveries, technology, know-how, methods, data, applications and products (in each case whether or not patentable) arising from the Research Program or otherwise related to the Program Compounds (collectively, the "Program Inventions") shall be exclusively owned by or assigned to Abbott and Abbott shall not divest or otherwise transfer any right, title or interest in or to any Program Inventions which would prevent or impair Abbott's ability to fulfill its obligations to John Hancock under this Agreement.

5.2 Patent Prosecution and Maintenance. Abbott will use Commercially Reasonable Efforts to obtain broad patent protection for the Program Inventions. Abbott shall be responsible for all costs and expenses and control all decisions related to filing for patent protection, including the preparation, filing (foreign and/or domestic), prosecution, issuance and maintenance of patent applications or patents covering Program Inventions.

5.3 Enforcement. Abbott shall have the sole right and authority to enforce the patents or any other rights arising from Program Inventions against any infringers. If Abbott initiates any action or lawsuit to enforce such patents or other rights, it shall be solely responsible for the cost and expense thereof. Abbott will promptly notify John Hancock at such time as it becomes aware of any infringement activities and of any such enforcement actions or lawsuit, and Abbott will provide information concerning them as reasonably requested by John Hancock. All moneys recovered upon the final judgment or settlement of any such action or lawsuit, less the out-of-pocket cost and expense thereof, shall be added to and included in the Net Sales (for the years in each Royalty Term with respect to which such action or lawsuit concerns); **provided that if such recovered moneys represent something other than Net Sales by the infringer (e.g., lost profits or a royalty), Abbott agrees to allocate a portion of the recovered moneys to John Hancock so as to approximate the appropriate royalty on Net Sales by the infringer during each year of the Royalty Terms. [Unclear on the intent of this provision?]**

## ARTICLE 6 MILESTONE PAYMENTS TO JOHN HANCOCK

CONFIDENTIAL  
JH 004400

6.1 Closing Fee. Upon execution of this Agreement, Abbott shall pay (\$\_\_\_\_\_) to John Hancock. Any payment here will exceed \$20 million?

-13-

6.2 Management Fee. On \_\_\_\_\_ 2001, 2002, 2003 and 2004, Abbott shall pay to John Hancock a management fee, each of which shall be in the amount of Two Million Dollars (\$2,000,000).

6.3 Milestone Notification and Payments. Abbott shall promptly notify John Hancock of the occurrence any of the following events that give rise to Abbott's obligation to make a milestone payment. Except as hereinafter limited, Abbott shall pay the following milestone payments to John Hancock in the amounts and at the times set forth below with respect to each Program Compound:

- (a) One Million Dollars (\$1,000,000) shall be paid within thirty (30) days after the allowance by the FDA of the first Investigational New Drug Application [define] for such Program Compound;
- (b) Two Million Dollars (\$2,000,000) shall be paid within thirty (30) days after the initiation of the first Phase I Clinical Trial with such Program Compound;
- (c) Three Million Dollars (\$3,000,000) shall be paid within thirty (30) days after the initiation of the first Phase II Clinical Trial with such Program Compound;
- (d) Four Million Dollars (\$4,000,000) shall be paid within thirty (30) days after the initiation of the first Phase III Clinical Trial with such Program Compound;
- (e) Five Million Dollars (\$5,000,000) shall be paid within thirty (30) days after the filing of the first NDA with the FDA for such Program Compound; and
- (f) Ten Million Dollars (\$10,000,000) shall be paid within thirty (30) days after the first Regulatory Approval of such Program Compound in the U.S. Territory.

The aggregate of milestone payments under Section 6.3(a), (b), (c), (d), and (e) for all Program Compounds shall be limited to Twelve Million Dollars (\$12,000,000), and once such aggregate limit has been paid, no further payments shall be due and payable under Sections 6.3(a), (b), (c), (d) or (e). The aggregate of milestone payments under Section 6.3(f) for all Program Compounds shall be limited to Forty Million Dollars (\$40,000,000), and once such aggregate limit has been paid, no further payments shall be due and payable under Section 6.3(f). The aggregate of milestone payments under Sections 6.3(a), (b), (c), (d) and (e) for all Program Compounds shall be limited to Three Million Dollars (\$3,000,000) during the first Program Year and shall be limited to Six Million Dollars (\$6,000,000) during the second Program Year, and once such annual limit has been reached for these particular Program Years, no further payments shall be due under Sections 6.3(a), (b), (c), (d) and (e) for the remainder of such Program Year; provided that any amounts that would have been due to John Hancock but for such annual limits shall be

CONFIDENTIAL  
JH 004401

-14-

paid in subsequent Program Years so long as the Program Compound to which it relates has not been abandoned, divested or out-licensed by Abbott. Further, the milestone payments set forth in Section 6.2 will not be made more than once with respect to any given Program Compound regardless of the number of such trials, filings or approvals that may be undertaken or granted with respect to such Program Compound, including, without limitation, multiple product forms of the same Program Compounds, additional active or inactive ingredients, indications, delivery modules and/or dosage strengths. Finally, a milestone payment shall only be made with respect to a milestone achieved after the date of this Agreement. For instance, if a Program Compound is in Phase III Clinical Trials at the Effective Date of this Agreement, then no milestones shall ever be paid under Sections 6.3(a), (b), (c) and (d) for such Program Compound regardless of whether the Program Compound were ever to achieve such milestones as part of a different development program for instance for a new dosage strength or new indication. Exhibit 6.3 sets forth the current stage of clinical development for each Program Compound.

#### ARTICLE 7 ROYALTIES

7.1 Royalty Rates. Subject to the limitation set forth below, Abbott shall pay to John Hancock royalties equal to the following percentages calculated on a calendar year to calendar year basis on the aggregate Net Sales of all Products in the Territory:

<u>Royalty percentage</u>	<u>Calendar year Net Sales (in millions) of all Products in the Territory</u>
8% of those Net Sales	up to \$400
and then 4% of those Net Sales	in excess of \$400 up to \$1,000
and then 1% of those Net Sales	in excess of \$1,000 up to \$2,000
and then .5% of those Net Sales	in excess of \$2,000

7.2 Royalty Term. The obligation to make royalty payments on each Product shall be calculated on a country-by-country basis, shall commence for such Product upon the First Commercial Sale thereof in such country, and shall last for the duration of the Royalty Term in each given country for such Product. Notwithstanding anything to the contrary herein, the obligation to make royalty payments on the Products shall not begin until [\_\_\_\_\_, 2002] [the commencement of the Third Program Year] (and with respect only to Net Sales occurring on or after such date) and shall cease at December 31, 2014.

#### ARTICLE 8 ROYALTY REPORTS AND ACCOUNTING

8.1 Reports, Exchange Rates. With respect to every Quarterly Reporting Period for which Abbott is obligated to pay a royalty hereunder, Abbott shall furnish to John Hancock a written report for such Quarterly Reporting Period within sixty (60) days of the end of such Quarterly Reporting Period [(that is, within sixty (60) days of each [March 31], [June 30], [September 30] and [December 31])] showing in reasonably specific detail:

CONFIDENTIAL  
JH 004402



-15-

- (a) the total gross sales in each country for each Product sold by Abbott, its Affiliates and Licensees in the Territory and the detailed calculation of Net Sales from gross sales in each country for each Product;
- (b) the royalties payable in Dollars, if any, which shall have accrued hereunder;
- (c) the dates of the First Commercial Sale of the Product in any country in the Territory during such Quarterly Reporting Period;
- (d) the exchange rates used in determining the amount of Dollars.
- (e) **[WITHHOLDING TAXES DELETED HERE - WHY?]**

With respect to sales of Products invoiced in Dollars, the gross sales, Net Sales (including all adjustments and deductions permitted to be made hereunder in calculating the same), and royalties payable shall be expressed in Dollars. With respect to sales of Products invoiced in a currency other than Dollars, the gross sales, Net Sales and royalties payable shall be expressed in their Dollar equivalent, calculated [using the Inter Bank rate set forth in the International Report published by International Reports Inc. as Foreign Exchange Rates quoted in New York on the day nearest the last business day of] [or the weighted average exchange rate on each day during ?] the Quarterly Reporting Period. [The gross sales made outside the U.S. Territory during a fiscal quarter will be reported with the gross sales made in the U.S. Territory during the calendar quarter in which the last month of the fiscal quarter falls.]

## 8.2 Audits.

- (a) Upon the written request of John Hancock and, in the absence of any breach by Abbott hereunder, not more than once in each calendar year, Abbott shall permit John Hancock and an independent certified public accounting firm of nationally recognized standing, selected by John Hancock and reasonably acceptable to Abbott, at John Hancock's expense, to have access during normal business hours to such of the records of Abbott, its Affiliates and Licensees to verify the accuracy of the royalty reports and the amounts and calculation of any payments required hereunder for any year ending not more than thirty-six (36) months prior to the date of such request.
- (b) If such accounting firm concludes that additional royalties or other payments were owed during such period, Abbott shall have the option to invoke the proceedings of Section 16.7 below or pay the additional royalties or other payments within thirty (30) days of the date John Hancock delivers to Abbott such accounting firm's written report so concluding. The reasonable fees and expenses charged by such accounting firm shall be paid by John Hancock; provided, however, if the audit discloses that the amounts payable by Abbott for any Quarterly Reporting

**CONFIDENTIAL**  
**JH 004403**

-16-

Period are more than one hundred five percent (105%) of the royalties actually paid for such period; then Abbott shall pay the reasonable fees and expenses charged by such accounting firm.

- (c) Abbott shall include in each license granted by it pursuant to this Agreement a provision requiring the Licensee (including any Affiliates of Abbott) to make reports to Abbott, to keep and maintain records of Net Sales made pursuant to such license and to grant access to such records by John Hancock and its accounting firm or other auditor to the same extent required of Abbott under this Agreement.
- (d) All reports and payments not disputed as to correctness by John Hancock within three (3) years after receipt thereof shall thereafter conclusively be deemed correct for all purposes, and Abbott and its Affiliates and licensees shall be released from any liability or accountability with respect to such royalties and payments.

8.3 Confidential Financial Information. John Hancock shall treat all information subject to review under this Article 8, and shall cause its accounting firm to agree to treat all such information, in accordance with the provisions of Article 10.

8.4 Accounting Principles. All accounting hereunder, including without limitation all determinations of gross sales, Net Sales (including all adjustments and deductions permitted to be made hereunder in calculating the same), Program Related Costs and all calculations underlying such determinations, shall be made in accordance with generally accepted accounting principles as in effect in the United States, consistently applied.

## ARTICLE 9 PAYMENTS

9.1 Payment Terms. With respect to every Quarterly Reporting Period for which Abbott is obligated to pay a royalty hereunder, such royalties shall be due and payable within sixty (60) days of the end of such Quarterly Reporting Period [(that is, within sixty (60) days of each [March 31], [June 30], [September 30] and [December 31])]. Payment of royalties in whole or in part may be made in advance of such due date.

9.2 Payment Method. All royalties and other payments by Abbott to John Hancock under this Agreement shall be made by bank wire transfer in immediately available funds in accordance with the instructions set forth on Exhibit 9.2 attached hereto or in accordance with such other instructions as John Hancock may give from time to time.

9.3 Withholding Taxes [TAX]. All amounts owing from Abbott to John Hancock under this Agreement shall be paid without deduction to account for any withholding taxes, value-added taxes or other taxes, levies or charges with respect to such amounts payable on behalf of Abbott, its Affiliates or Licensees and any taxes required to be withheld on behalf of Abbott, its Affiliates or Licensees in any country within the Territory.

CONFIDENTIAL  
JH 004404

-17-

9.4 Late Payments. Abbott shall pay interest to John Hancock on the aggregate amount of any payments by Abbott that are not paid on or before the date such payments are due under this Agreement, including, without limitation, any disputed payments or payments resulting from any audit, at a rate per annum equal to the lesser of (a) the prime rate of interest plus \_\_\_\_ basis points as reported by \_\_\_\_ bank in \_\_\_\_\_, from time to time (with any change in such reported rate being effective immediately for purposes hereof), or (b) the highest rate permitted by applicable law, calculated on the number of days such payments is delinquent until paid in full in cash. All such amounts shall be payable upon demand.

## ARTICLE 10 CONFIDENTIALITY

10.1 Nondisclosure Obligations. Except as otherwise provided in this Article 10, during the term of the Agreement and for a period of ten (10) years thereafter, (a) John Hancock shall maintain in confidence in accordance with such procedures as are adopted by John Hancock to protect its own confidential information and shall use only for purposes of this Agreement (including, without limitation, enforcement of the terms hereof), information and data related to the Program Compounds or Products; and (b) John Hancock shall also maintain in confidence in accordance with such policies, and use only for purposes of this Agreement, all information and data supplied by Abbott under this Agreement, which if disclosed in writing is marked "confidential", if disclosed orally is promptly thereafter summarized and confirmed in writing to the other party and marked "confidential", or if disclosed in some other form is marked "confidential."

10.2 Permitted Disclosures. For purposes of this Article 10, information and data described in clause (a) or (b) above shall be referred to as "Confidential Information". John Hancock may disclose Confidential Information as required by applicable law, regulation or judicial process, provided that John Hancock shall, if legally permitted, give Abbott prompt written notice thereof. The obligation not to disclose or use Confidential Information shall not apply to any part of such Confidential Information that (i) is or becomes patented, published or otherwise part of the public domain other than by acts or omissions of John Hancock in contravention of this Agreement; or (ii) is disclosed to John Hancock by a third party, provided such Confidential Information was not obtained on a confidential basis by such third party from Abbott, its Affiliates or Licensees; or (iii) prior to disclosure under the Agreement, was already in the possession of John Hancock, provided such Confidential Information was not obtained directly or indirectly from Abbott, its Affiliates or Licensees under an ongoing obligation of confidentiality; or (iv) is disclosed in a press release agreed to by both parties under Section 10.3 below.

10.3 Publicity Review. Without the prior written consent of the other party, neither party shall make any statement to the public regarding the execution and/or any other aspect of the subject matter of this Agreement or any work under the Research Program. John Hancock and Abbott shall not disclose any terms or conditions of this Agreement to any third party without the prior consent of the other party, except as set forth above in this Section 10.3 or as

CONFIDENTIAL  
JH 004405



-18-

required by applicable law, regulation or court order. The parties have agreed not to issue a press release announcing the execution of this Agreement.

## ARTICLE 11 TERM AND TERMINATION

11.1 Expiration. Unless terminated earlier by agreement of the parties or pursuant to Sections 11.2 or 11.4 below, this Agreement shall expire upon satisfaction of Abbott's obligations to pay royalties and all other amounts under this Agreement.

11.2 Material Breach. It is the parties' express intent that consideration shall first and foremost be given to remedying any breach of this Agreement through the payment of monetary damages or such other legal or equitable remedies as shall be appropriate under the circumstances and that there shall only be a limited right to terminate this Agreement under the following circumstances as a matter of last resort. In the event that the Neutral, in accordance with the procedures set forth in Section 16.7, has rendered a ruling that a party has breached this Agreement, which ruling specified the remedies imposed on such breaching party for such breach (the "Adverse Ruling"), and the breaching party has failed to comply with the terms of the Adverse Ruling within the time period specified therein for compliance, or if such compliance cannot be fully achieved by such date, or if the breaching party has failed to commence compliance and/or has failed to use diligent efforts to achieve full compliance as soon after the Adverse Ruling as is reasonably possible, then the non-breaching party shall have the following rights and all other rights available to it under law:

- (a) where Abbott is the breaching party that failed to comply with the Adverse Ruling and where the basis for such breach is Abbott's failure to abide by a material obligation under this Agreement, John Hancock may, upon written notice to Abbott, terminate this Agreement; and
- (b) where John Hancock is the breaching party that failed to comply with the Adverse Ruling and where the basis for such breach is John Hancock's failure to abide by a material obligation under this Agreement, Abbott may, upon written notice to John Hancock, terminate this Agreement.

11.3 Effect of Expiration or Termination. Expiration or termination of this Agreement shall not relieve the parties of any obligation accruing prior to such expiration or termination. The provisions of Articles 10 through 12, 15 and 16 shall survive the expiration or termination of the Agreement.

## ARTICLE 12 WARRANTIES AND INDEMNITY

12.1 John Hancock Representations and Warranties. John Hancock represents and warrants to Abbott that:

CONFIDENTIAL  
JH 004406

-19-

- (a) The execution and delivery of this Agreement and the performance of the transactions contemplated hereby have been duly authorized by all appropriate John Hancock corporation action. This Agreement constitutes John Hancock's valid and binding legal obligation, enforceable against it in accordance with its terms.
- (b) The performance by John Hancock of any of the terms and conditions of this Agreement on its part to be performed does not and will not constitute a breach or violation of its organizational documents or any other material agreement or understanding, written or oral, to which it is a party or any law, statute, rule or regulation by which it is bound.
- (c) No consent, approval, license or authorization of, or designation, declaration or filing with, any court or governmental authority is or will be required on the part of John Hancock in connection with the execution, delivery and performance by John Hancock of this Agreement or any other agreements or instruments executed and delivered by John Hancock in connection herewith or therewith, including, without limitation, any filings pursuant to federal or state securities laws or pursuant to any federal or foreign anti-trust laws.
- (d) Neither John Hancock nor any person acting on its behalf (i) has taken or will take any action which would subject this Agreement and the consummation of the transactions contemplated hereby to the registration or qualification requirements of any foreign or domestic (federal or state) securities laws, (ii) has dealt with any broker, finder or other similar person in connection with the transactions contemplated by this Agreement or (iii) is under any obligation to pay any broker's fee, finder's fee or commission in connection with such transactions.

12.2 Abbott Representations and Warranties: Abbott represents and warrants to John Hancock that as of the Effective Date: [to be discussed - delivery of opinion of counsel with respect to certain of the following topics]

- (a) The execution and delivery of this Agreement and the performance of the transactions contemplated hereby have been duly authorized by all appropriate Abbott Corporation action. This Agreement constitutes Abbott's valid and binding legal obligation, enforceable against it in accordance with its terms.
- (b) The performance by Abbott of any of the terms and conditions of this Agreement on its part to be performed does not and will not constitute a breach or violation of its organizational documents or any other agreement or understanding, written or oral, to which it is a party or any law, statute, rule or regulation by which it is bound.

CONFIDENTIAL  
JH 004407

-20-

- (c) [FDA hereunder?] No consent, approval, license or authorization of, or designation, declaration or filing with, any court or governmental authority is or will be required on the part of Abbott in connection with the execution, delivery and performance by Abbott of this Agreement or any other agreements or instruments executed and delivered by Abbott in connection herewith or therewith, including, without limitation, any filings pursuant to federal or state securities laws or pursuant to any federal or foreign anti-trust laws.
- (d) Set forth on Exhibit 12.2(d) is the full name, detailed description of the stage of development, and current status for each Program Compound.
- (e) **[Patent Department review pending]** Set forth on Exhibit 12.2(e) is a list and description of all material domestic and foreign patents, patent rights, patent applications and all patent applications that are in the process of being prepared that are owned by or registered in the name of Abbott, or of which Abbott is a licensor or licensee or in which Abbott has any right, which cover any of the Program Compounds. To the knowledge of Abbott, all of such patents and patent applications have been duly filed in or issued by the United States Patent and Trademark Office or the equivalent foreign patent office, as the case may be, and have been properly maintained and renewed in accordance with all applicable laws and regulations. To the knowledge of Abbott, Abbott owns or has a valid license to all Program Inventions, patents, patent applications, copyrights, manufacturing processes, formulae, trade secrets, proprietary rights and know how necessary with respect to the Program Compounds and the Research Program as heretofore conducted and as proposed to be conducted (collectively, the "Intellectual Property"). Except as set forth in Exhibit 12.2(e), Abbott's use of the Intellectual Property does not require the consent of any other person and the Intellectual Property is owned exclusively by Abbott, free and clear of any liens or encumbrances of any other person. Except as set forth in Exhibit 12.2(e), Abbott has not received any communications alleging that, and no claim is pending or, to the knowledge of Abbott, threatened to the effect that, the operations of Abbott with respect to the Research Program or the Program Compounds infringe upon or conflict with (or will infringe or conflict with) the asserted rights of any other person under any domestic or foreign patent, trademark, service mark, copyright, trade secret, proprietary right or any other intellectual property right. Except as set forth in Exhibit 12.2(e), no claim is pending or, to the knowledge of Abbott, threatened to the effect that any of the Intellectual Property is invalid or unenforceable by Abbott, and there is no basis known to Abbott. To the knowledge of Abbott, all technical information developed by and belonging to Abbott which has not been patented or copyrighted has been kept confidential.
- (f) Except pursuant to the Eisai Agreement, Abbott has not granted any other

CONFIDENTIAL  
JH 004408

-21-

person the right to sell the Program Compounds.

- (g) To the knowledge of Abbott and with respect to the Research Program and each of the Program Compounds, Abbott is not now, and in performing its obligations hereunder will not be, in any way making an unlawful or wrongful use of any confidential information, know-how, or trade secrets of any other person, including without limitation, any present or past employee of Abbott.
- (h) Neither this Agreement nor any Exhibit to this Agreement, contains any untrue statement of material fact or omits to state any material fact necessary to make the statements contained herein or therein not misleading. There is no fact known to Abbott as of the date of this Agreement that has not been disclosed herein or in any other agreement, document or written statement furnished by Abbott to John Hancock or its counsel in connection with the transactions contemplated hereby which Abbott reasonably believes has had or would have a material adverse affect on the current status (safety, efficacy, or scientific viability) of the Research Program or any of the Program Compounds.
- (i) Neither Abbott nor any person acting on its behalf (i) has taken or will take any action which would subject this Agreement and the consummation of the transactions contemplated hereby to the registration or qualification requirements of any foreign or domestic (federal or state) securities laws; (ii) has dealt with any broker, finder or other similar person in connection with the transactions contemplated by this Agreement or (iii) is under any obligation to pay any broker's fee, finder's fee or commission in connection with such transactions.
- (j) There is no action, proceeding or investigation pending or, to the knowledge of Abbott, threatened which (i) questions the validity of this Agreement or any action taken or to be taken by Abbott pursuant thereto or (ii) which has resulted in, or could reasonably be expected to result in, a material adverse change in the prospects or condition (safety, efficacy, scientific viability or other) of the Research Program or any of the Program Compounds.
- (k) With respect to the Research Program and each of the Program Compounds, Abbott has (and in the future will have) obtained, to the extent permitted by law, from each of its employees and from each of the employees of its Affiliates an agreement in customary form pursuant to which each such person shall have agreed that all title to the Program Inventions, Program Compounds and Products is and shall be held by Abbott.

CONFIDENTIAL  
JH 004409

-22-

12.3 No Conflict. Abbott and John Hancock represent and warrant that this Agreement does not, and will not, conflict with any other right or obligation provided under any other agreement or obligation that Abbott or John Hancock has with or to any third party.

12.4 Compliance with Law. Abbott represents and warrants to John Hancock that it will comply with all applicable laws, regulations and guidelines in connection with its performance of its obligations and rights pursuant to this Agreement, including the regulations of the United States and any other relevant nation concerning any export or other transfer of technology, services or products.

[12.5 Certain Breaches. As mentioned in our memo, in the event of certain breaches, we feel that John Hancock should be entitled to certain remedies - to be discussed.] EACH PARTY TO THIS AGREEMENT AGREES THAT, EXCEPT FOR THE REPRESENTATIONS AND WARRANTIES CONTAINED IN THIS AGREEMENT, NEITHER PARTY MAKES ANY OTHER REPRESENTATIONS OR WARRANTIES, AND EACH HEREBY DISCLAIMS ANY OTHER REPRESENTATIONS OR WARRANTIES MADE BY ITSELF OR ANY OF ITS OFFICERS, DIRECTORS, EMPLOYEES, AGENTS, FINANCIAL AND LEGAL ADVISORS OR OTHER REPRESENTATIVES, WITH RESPECT TO THE EXECUTION AND DELIVERY OF THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED BY THIS AGREEMENT, NOTWITHSTANDING THE DELIVERY OR DISCLOSURE TO THE OTHER OR THE OTHER'S REPRESENTATIVES OF ANY DOCUMENTATION OR OTHER INFORMATION WITH RESPECT TO ANY ONE OR MORE OF THE FOREGOING.

12.6 Indemnification of John Hancock. Abbott shall indemnify and hold John Hancock and its Affiliates, agents, directors and employees harmless, and hereby forever releases and discharges John Hancock and its Affiliates, agents, directors and employees, from and against all Losses related to or arising out of, directly or indirectly, (a) any negligence, recklessness or intentional misconduct of Abbott or its Affiliates, agents, directors, employees, Subcontractors, licensees (including Licensees) or sublicensees in connection with the Research Program, Program Compounds or Products, or (b) any manufacture, use, storage, distribution or sale of the Program Compounds or Products by anyone, including without limitation all Losses related to any personal injury or death, or (c) any breach by Abbott its representations, warranties or obligations hereunder or (d) the consummation of the transactions contemplated hereby, except, in each case, to the extent any such Losses are the result of any breach by John Hancock of its representations, warranties or obligations hereunder.

12.7 Procedure. If John Hancock or any of its Affiliates, agents, directors or employees (each, an "Indemnitee") intends to claim indemnification under this Article 12, it shall promptly notify Abbott (the "Indemnitor") of any Loss or action in respect of which the Indemnitee intends to claim such indemnification, and the Indemnitor shall have the right to participate in, and, to the extent the Indemnitor so desires, to assume the defense thereof with counsel selected by the Indemnitor; provided, however, that an Indemnitee shall have the right to retain its own counsel, with the fees and expenses of such counsel to be paid by the Indemnitor, if representation of such Indemnitee by the counsel retained by the Indemnitor would be inappropriate due to actual or potential differing interests between such Indemnitee and any other party represented by such counsel in such proceedings. The indemnity obligation in this Article 12 shall not apply to amounts paid in settlement of any loss, claim, damage, liability or action if

CONFIDENTIAL  
JH 004410



-23-

such settlement is effected without the consent of the Indemnitor, which consent shall not be withheld unreasonably or delayed. The failure to deliver notice to the Indemnitor within a reasonable time after the commencement of any such action, if materially prejudicial to its ability to defend such action, shall relieve the Indemnitor of any liability to the Indemnitee under this Article 12, but the omission so to deliver notice to the Indemnitor will not relieve it of any liability that it may have to any Indemnitee otherwise than under this Article 12. The Indemnitee shall cooperate fully with the Indemnitor and its legal representatives in the investigation of any action, claim or liability covered by indemnification under this Article 12, at the expense of the Indemnitor.

12.8 Insurance. Abbott shall at its expense maintain, through self-insurance or otherwise, product liability insurance with respect to the development, manufacture, sale and use of Products and Program Compounds in such amounts and on such terms as Abbott customarily maintains with respect to its other similar products. Abbott shall maintain such insurance for so long as it continues to develop, manufacture or sell any Products or Program Compounds, and thereafter for so long as Abbott customarily currently maintains such insurance.

12.9 Survival. The representations and warranties set forth in this Agreement shall survive the Execution Date.

### ARTICLE 13 FORCE MAJEURE

Neither party shall be held liable or responsible to the other party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party including but not limited to fire, floods, embargoes, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, acts of God or acts, omission or delays in acting by any governmental authority.

### ARTICLE 14 ASSIGNMENT

Except as expressly provided hereunder, this Agreement may not be assigned or otherwise transferred, nor may any right or obligations hereunder be assigned or transferred by either party without the consent of the other party; provided, however, that either party shall be obligated to assign this Agreement and its rights and obligations hereunder in connection with the transfer or sale of all or substantially all of its business pertaining to this Agreement, or in the event of its merger or consolidation or change in control or similar transaction and in such event such party shall cause its successor or transferee in such transaction to assume all of the obligations of such party. [Why is this necessary? What if 20 assignees?] Any permitted assignee shall assume all obligations of its assignor under this Agreement. Notwithstanding the foregoing, John Hancock shall have right to assign its right to payments without Abbott's consent, in whole or in part, hereunder (but not its obligations) to any other person and such other

CONFIDENTIAL  
JH 004411

-24-

person shall be permitted to enjoy and exercise all of the rights of John Hancock assigned to it; provided that if such assignee is located outside the United States, (i) John Hancock shall notify Abbott at least sixty (60) days in advance and (ii) such payment shall be subject to any applicable U.S. withholding and (iii) such assignee shall not be a company in the health care industry.

**ARTICLE 15**  
**SEVERABILITY**

Each party hereby agrees that it does not intend its execution and delivery hereof or its performance hereunder to violate any public policy, statutory or common laws, rules, regulations, treaty or decision of any government agency or executive body thereof of any country or community or association of countries. If any term or provision of this Agreement is held to be invalid, illegal or unenforceable by a court or other governmental authority of competent jurisdiction, such invalidity, illegality or unenforceability shall not affect any other term or provision of this Agreement, which shall remain in full force and effect. The holding of a term or provision to be invalid, illegal or unenforceable in a jurisdiction shall not have any effect on the application of the term or provision in any other jurisdiction.

**ARTICLE 16**  
**MISCELLANEOUS**

16.1 **Notices.** Any consent, notice or report required or permitted to be given or made under this Agreement by one of the parties hereto to the other shall be in writing, delivered personally or by facsimile (and promptly confirmed by personal delivery, U.S. first class mail or courier), U.S. first class mail or courier, postage prepared (where applicable), addressed to such other party at its address indicated below, or to such other address as the addressee shall have last furnished in writing to the addressor and (except as otherwise provided in this Agreement) shall be effective upon receipt by the addressee.

If to John Hancock: John Hancock Life Insurance Company  
200 Clarendon Street, T-57  
Boston, MA 02117  
Attention: Bond & Corporate Finance Group  
Telephone: \_\_\_\_\_  
Fax: 617-572-1628

copy to: John Hancock Life Insurance Company  
200 Clarendon Street, T-50  
Boston, MA 02117  
Attention: Investment Law Division  
Telephone: \_\_\_\_\_  
Fax: 617-572-9268

**CONFIDENTIAL**  
**JH 004412**

-25-

If to Abbott:

Abbott Laboratories  
Dept. 309, Bldg. AP30  
200 Abbott Park Road  
Abbott Park, IL 60064-3537  
Attention: President, Pharmaceutical  
Products Division  
Telephone: 847-938-6863  
Fax: 847-938-5383

copy to:

General Counsel  
Abbott Laboratories  
Dept. 364, Bldg. AP6D  
100 Abbott Park Road  
Abbott Park, IL 60064-6020  
Telephone: 847-937-8905  
Fax: 847-938-6277

16.2 Applicable Law. The Agreement shall be governed by and construed in accordance with the internal laws of the State of Illinois. Abbott, to the extent that it may lawfully do so, hereby consents to service of process, and to be sued, in the Commonwealth of Massachusetts and consents to the exclusive jurisdiction of the courts of the Commonwealth of Massachusetts and the United States District Court for the District of Massachusetts, as well as to the jurisdiction of all courts to which an appeal may be taken from such courts, for the purpose of any suit, action or other proceeding arising out of any of its obligations hereunder or thereunder or with respect to the transactions contemplated hereby or thereby, and expressly waives any and all objections it may have as to venue in any such courts. Abbott further agrees that a summons and complaint commencing an action or proceeding in any of such courts shall be properly served and shall confer personal jurisdiction if served personally or by certified mail to it at its address for notices as provided in this Agreement or as otherwise provided under the laws of the Commonwealth of Massachusetts. THE PARTIES EACH IRREVOCABLY WAIVE ALL RIGHT TO A TRIAL BY JURY IN ANY SUIT, ACTION OR OTHER PROCEEDING INSTITUTED BY OR AGAINST IT IN RESPECT OF ITS OBLIGATIONS HEREUNDER OR THEREUNDER OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THEREBY.

16.3 Entire Agreement. This Agreement contains the entire understanding of the parties with respect to the subject matter hereof. All express or implied agreements and understandings, either oral or written, with respect to the subject matter hereof heretofore made are expressly merged in and made a part of this Agreement. This Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by both parties hereto.

16.4 Headings. The captions to the several Articles and Sections thereof are not a part of this Agreement, but are merely guides or labels to assist in locating and reading the several Articles and Sections hereof.

16.5 Independent Contractors. It is expressly agreed that John Hancock and Abbott shall be independent contractors and that the relationship between the two parties shall not constitute a partnership, joint venture or agency. Neither John Hancock nor Abbott shall have

CONFIDENTIAL  
JH 004413



-26-

the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on the other, without the prior consent of the other party to do so.

16.6 Performance By Affiliates, Licensees and Subcontractors. The parties recognize that Abbott may carry out certain obligations under this Agreement through performance by its Affiliates, Licensees and Subcontractors (but in no event shall that relieve Abbott of any of its obligations hereunder). Abbott guarantees that the activities of its Affiliates, Licensees and Subcontractors under this Agreement shall comply with this Agreement.

16.7 Alternative Dispute Resolution. The parties shall attempt to amicably resolve disputes arising between them regarding the validity, construction, enforceability or performance of the terms of this Agreement, and any differences or disputes in the interpretation of the rights, obligations, liabilities and/or remedies hereunder, which have been identified in a written notice from one party to the other, by good faith settlement discussions between the President of Abbott's Pharmaceutical Products Division and the Managing Director of John Hancock or his designee. The parties agree that any dispute that arises in connection with this Agreement, which cannot be amicably resolved by such representatives within thirty (30) days after the receipt of such written notice, shall be resolved by binding Alternative Dispute Resolution ("ADR") in the manner described in Exhibit 16.7 attached hereto.

16.8 Waiver. The waiver by either party hereto of any right hereunder or the failure to perform or of a breach by the other party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by said other party whether of a similar nature or otherwise.

16.9 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

[the remainder of this page is intentionally blank]

CONFIDENTIAL  
JH 004414

-27-

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first set forth above.

JOHN HANCOCK LIFE  
INSURANCE COMPANY

ABBOTT LABORATORIES

By: \_\_\_\_\_

By: \_\_\_\_\_

Name: \_\_\_\_\_

Name: \_\_\_\_\_

Title: \_\_\_\_\_

Title: \_\_\_\_\_

CONFIDENTIAL  
JH 004415

-28-

EXHIBIT 1.           

ANNUAL RESEARCH PLAN - FIRST PROGRAM YEAR

CONFIDENTIAL  
JH 004416

-29-

EXHIBIT 1. \_\_

PROGRAM COMPOUNDS

ABT 980 - BPH Back-up (phase III)  
ABT 627 - Prostate and other cancer (phase III)  
ABT 773 - Oral/pediatric/IV (late phase II)  
ABT 594 - Neurological/bone/acute pain (late phase II)  
E7010 - Cancer (phase II)  
ABT 518 - Cancer (phase I)  
FTI - Cancer (late preclinical)  
Urokinase - Cancer (preclinical)

CONFIDENTIAL  
JH 004417

-30-

## EXHIBIT 16.7

## ALTERNATIVE DISPUTE RESOLUTION

The parties recognize that a bona fide dispute as to certain matters may arise from time to time during the term of this Agreement which relates to either party's rights and/or obligations. To have such a dispute resolved by this Alternative Dispute Resolution ("ADR") provision, a party first must send written notice of the dispute to the other party for attempted resolution by good faith negotiations between the Managing Director of John Hancock and the Senior Vice President, Pharmaceutical Products Division, of Abbott (or their equivalents) of the affected subsidiaries, divisions, or business units within thirty (30) days after such notice is received (all references to "days" in this ADR provision is to calendar days).

Any negotiations regarding a dispute shall be treated as settlement negotiations for purposes of the Federal Rules of Evidence and any similar state rules of evidence. Such negotiations shall not be admissible in any subsequent ADR hearing.

If the matter has not been resolved within thirty (30) days of the notice of dispute, or if the parties fail to meet within such thirty (30) days, either party may initiate an ADR proceeding as provided herein. The parties shall have the right to be represented by counsel in such a proceeding.

1. To begin an ADR proceeding, a party shall provide written notice to the other party of the issues to be resolved by ADR. Within fourteen (14) days after its receipt of such notice, the other party may, by written notice to the party initiating the ADR, add additional issues to be resolved within the same ADR.

2. Within twenty-one (21) days following receipt of the original ADR notice, the parties shall select a mutually acceptable neutral to preside in the resolution of any disputes in this ADR proceeding. If the parties are unable to agree on a mutually acceptable neutral within such period, the parties shall request the President of the Center for Public Resources ("CPR"), 366 Madison Avenue, New York, New York 10017 to select a neutral pursuant to the following procedures:

(a) The CPR shall submit to the parties a list of not less than five (5) candidates within fourteen (14) days after receipt of the request from the parties, along with a Curriculum Vitae for each candidate. No candidate shall be an employee, director, or shareholder of either party or any of their subsidiaries or affiliates.

(b) Such list shall include a statement of disclosure by each candidate of any circumstances likely to affect his or her impartiality.

(c) Each party shall number the candidates in order of preference (with the number one (1) signifying the greatest preference) and shall deliver the list to the CPR within seven (7) days following receipt of the list of candidates. If a party believes a conflict of interest exists regarding any of the candidates, that party shall provide a written explanation of the conflict to the CPR along with its list showing its order of preference for the candidates. Any party failing to return a list of preferences on time shall be deemed to have no order of preference.

CONFIDENTIAL  
JH 004418

-31-

(d) If the parties collectively have identified fewer than three (3) candidates deemed to have conflicts, the CPR immediately shall designate as the neutral the candidate for whom the parties collectively have indicated the greatest preference. If a tie should result between two candidates, the CPR may designate either candidate. If the parties collectively have identified three (3) or more candidates deemed to have conflicts, the CPR shall review the explanations regarding conflicts and, in its sole discretion, may either (i) immediately designate as the neutral the candidate for whom the parties collectively have indicated the greatest preference, or (ii) issue a new list of not less than five (5) candidates, in which case the procedures set forth in subparagraphs 2(a) - 2(d) shall be repeated.

3. No earlier than twenty-eight (28) days or later than fifty-six (56) days after selection, the neutral shall hold a hearing to resolve each of the issues identified by the parties. The ADR proceeding shall take place in \_\_\_\_\_, or at such other location agreed upon by the parties. The language of the ADR shall be English.

4. At least seven (7) days prior to the hearing, each party shall submit the following to the other party and the neutral:

- (a) a copy of all exhibits on which such party intends to rely in any oral or written presentation to the neutral;
- (b) a list of any witnesses such party intends to call at the hearing, and a short summary of the anticipated testimony of each witness;
- (c) a proposed ruling on each issue to be resolved, together with a request for a specific damage award or other remedy for each issue. The proposed rulings and remedies shall not contain any recitation of the facts or any legal arguments and shall not exceed one (1) page per issue.
- (d) a brief in support of such party's proposed rulings and remedies, provided that the brief shall not exceed twenty (20) pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

Except as expressly set forth in subparagraphs 4(a) - 4(d), no discovery shall be required or permitted by any means, including depositions, interrogatories, requests for admissions, or production of documents.

5. The hearing shall be conducted on two (2) consecutive days and shall be governed by the following rules:

- (a) Each party shall be entitled to five (5) hours of hearing time to present its case. The neutral shall determine whether each party has had the five (5) hours to which it is entitled.
- (b) Each party shall be entitled, but not required, to make an opening statement, to present regular and rebuttal testimony, documents or other evidence, to cross-examine witnesses, and to make a closing argument. Cross-examination of witnesses shall occur immediately after their

CONFIDENTIAL  
JH 004419

-32-

direct testimony, and cross-examination time shall be charged against the party conducting the cross-examination.

(c) The party initiating the ADR shall begin the hearing and, if it chooses to make an opening statement, shall address not only issues it raised but also any issues raised by the responding party. The responding party, if it chooses to make an opening statement, also shall address all issues raised in the ADR. Thereafter, the presentation of regular and rebuttal testimony and documents, other evidence, and closing arguments shall proceed in the same sequence.

(d) Except when testifying, witnesses shall be excluded from the hearing until closing arguments.

(e) Settlement negotiations shall not be admissible under any circumstances. Affidavits prepared for purposes of the ADR hearing also shall not be admissible. As to all other matters, the neutral shall have sole discretion regarding the admissibility of any evidence.

6. Within seven (7) days following completion of the hearing, each party may submit to the other party and the neutral a post-hearing brief in support of its proposed rulings and remedies, provided that such brief shall not contain or discuss any new evidence and shall not exceed ten (10) pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

7. The neutral shall rule on each disputed issue within fourteen (14) days following completion of the hearing. Such ruling shall adopt in its entirety the proposed ruling and remedy of one of the parties on each disputed issue but may adopt one party's proposed rulings and remedies on some issues and the other party's proposed rulings and remedies on other issues. The neutral shall not issue any written opinion or otherwise explain the basis of the ruling.

8. The neutral shall be paid a reasonable fee plus expenses. These fees and expenses, along with the reasonable legal fees and expenses of the prevailing party (including all expert witness fees and expenses), the fees and expenses of a court reporter, and any expenses for a hearing room, shall be paid as follows:

(a) If the neutral rules in favor of one party on all disputed issues in the ADR, the losing party shall pay 100% of such fees and expenses.

(b) If the neutral rules in favor of one party on some issues and the other party on other issues, the neutral shall issue with the rulings a written determination as to how such fees and expenses shall be allocated between the parties. The neutral shall allocate fees and expenses in a way that bears a reasonable relationship to the outcome of the ADR, with the party prevailing on more issues, or on issues of greater value or gravity, recovering a relatively larger share of its legal fees and expenses.

9. The rulings of the neutral and the allocation of fees and expenses shall be binding, non-reviewable, and non-appealable, and may be entered as a final judgment in any court having jurisdiction.

CONFIDENTIAL  
JH 004420



-33-

10. Except as provided in paragraph 9 or as required by law, the existence of the dispute, any settlement negotiations, the ADR hearing, any submissions (including exhibits, testimony, proposed rulings, and briefs), and the rulings shall be deemed Confidential Information. The neutral shall have the authority to impose sanctions for unauthorized disclosure of Confidential Information.

CONFIDENTIAL  
JH 004421





CHS Draft 10/4/0010/17/00 |

RESEARCH FUNDING AGREEMENT

by and between

ABBOTT LABORATORIES, ~~[INC.]~~ |

and

JOHN HANCOCK LIFE INSURANCE COMPANY

dated as of

October \_\_, 2000

CONFIDENTIAL  
JH 004422

-i-

TABLE OF CONTENTS

<b>ARTICLE I - DEFINITIONS</b>	<b>1</b>
<b>ARTICLE 2 - ANNUAL RESEARCH PROGRAM</b>	<b>8</b>
2.1 <u>PROGRAM TERM</u>	8
2.2 <u>RESEARCH PLAN</u>	8
2.3 <u>CONDUCT OF RESEARCH</u>	8
2.4 <u>SUBCONTRACTING RESEARCH</u>	9
2.5 <u>RESEARCH REPORTS AND RECORDS</u>	9
<b>ARTICLE 3 - RESEARCH FUNDING</b>	<b>9</b>
3.1 <u>JOHN HANCOCK PROGRAM PAYMENTS</u>	9
3.2 <u>ABBOTT PROGRAM PAYMENTS</u>	10
3.3 <u>CARRYOVER PROVISIONS</u>	10
3.4 <u>TERMINATION OF JOHN HANCOCK'S PROGRAM PAYMENT OBLIGATION</u>	11
3.5 <u>HANCOCK FUNDING OBLIGATION</u>	11
<b>ARTICLE 4 - PRODUCT RESEARCH AND DEVELOPMENT</b>	<b>11</b>
4.1 <u>COMMERCIALLY REASONABLE EFFORTS</u>	11
4.2 <u>MARKETING AND SALE RESPONSIBILITY</u>	12
4.3 <u>FAILURE OF PROGRAM COMPOUND TO PROGRESS</u>	13
4.4 <u>COMPOUND ABT-627</u>	14
4.5 <u>ARM'S-LENGTH</u>	14
<b>ARTICLE 5 - PROGRAM INVENTIONS</b>	<b>14</b>
5.1 <u>OWNERSHIP</u>	14
5.2 <u>PATENT PROSECUTION AND MAINTENANCE</u>	14
5.3 <u>ENFORCEMENT</u>	14
<b>ARTICLE 6 - MILESTONE PAYMENTS TO JOHN HANCOCK</b>	<b>15</b>
6.1 <u>CLOSING FEE</u>	15
6.2 <u>MANAGEMENT FEE</u>	15
6.3 <u>MILESTONE NOTIFICATION AND PAYMENTS</u>	15
<b>ARTICLE 7 - ROYALTIES</b>	<b>16</b>
7.1 <u>ROYALTY RATES</u>	16
7.2 <u>ROYALTY TERM</u>	17
<b>ARTICLE 8 - ROYALTY REPORTS AND ACCOUNTING</b>	<b>17</b>
8.1 <u>REPORTS, EXCHANGE RATES</u>	17
8.2 <u>AUDITS</u>	18
8.3 <u>CONFIDENTIAL FINANCIAL INFORMATION</u>	19
8.4 <u>ACCOUNTING PRINCIPLES</u>	19
<b>ARTICLE 9 - PAYMENTS</b>	<b>19</b>
9.1 <u>PAYMENT TERMS</u>	19
9.2 <u>PAYMENT METHOD</u>	19
9.3 <u>WITHHOLDING TAXES</u>	19

24668323

**CONFIDENTIAL**  
**JH 004423**

-ii-

9.4	<u>LATE PAYMENTS</u>	19
<b>ARTICLE 10 - CONFIDENTIALITY</b>		<b>20</b>
10.1	<u>NONDISCLOSURE OBLIGATIONS</u>	20
10.2	<u>PERMITTED DISCLOSURES</u>	20
10.3	<u>PUBLICITY REVIEW</u>	20
<b>ARTICLE 11- TERM AND TERMINATION</b>		<b>20</b>
11.1	<u>EXPIRATION</u>	21
11.2	<u>MATERIAL BREACH</u>	21
11.3	<u>EFFECT OF EXPIRATION OF TERMINATION</u>	21
<b>ARTICLE 12 - WARRANTIES AND INDEMNITY</b>		<b>22</b>
12.1	<u>JOHN HANCOCK REPRESENTATIONS AND WARRANTIES</u>	22
12.2	<u>ABBOTT REPRESENTATIONS AND WARRANTIES</u>	22
12.3	<u>NO CONFLICT</u>	26
12.4	<u>COMPLIANCE WITH LAW</u>	26
12.5	<u>CERTAIN BREACHES</u>	26
12.6	<u>INDEMNIFICATION OF JOHN HANCOCK</u>	26
12.7	<u>PROCEDURE</u>	26
12.8	<u>INSURANCE</u>	27
12.9	<u>SURVIVAL</u>	27
<b>ARTICLE 13 - FORCE MAJEURE</b>		<b>27</b>
<b>ARTICLE 14 - ASSIGNMENT</b>		<b>27</b>
<b>ARTICLE 15 - SEVERABILITY</b>		<b>28</b>
<b>ARTICLE 16 - MISCELLANEOUS</b>		<b>28</b>
16.1	<u>NOTICES</u>	28
16.2	<u>APPLICABLE LAW</u>	29
16.3	<u>ENTIRE AGREEMENT</u>	29
16.4	<u>HEADINGS</u>	30
16.5	<u>INDEPENDENT CONTRACTORS</u>	30
16.6	<u>PERFORMANCE BY AFFILIATES</u>	30
16.7	<u>ALTERNATIVE DISPUTE RESOLUTION</u>	30
16.8	<u>WAIVER</u>	30
16.9	<u>COUNTERPARTS</u>	30

EXHIBIT 1.:	Annual Research Plan - First Program Year
EXHIBIT 1.:	List of Program Compounds
EXHIBIT 6.:	Program Compound Status
EXHIBIT 9.2:	Wiring Instructions for John Hancock
EXHIBIT 12.2(d):	Program Compound Detail
EXHIBIT 12.2(e):	Patents, etc.
EXHIBIT 16.7:	Alternative Dispute Resolution

**CONFIDENTIAL**  
**JH 004424**

~~CHS Draft 10/4/00~~ Abbott Draft 10/13/00

RESEARCH FUNDING AGREEMENT

This Research Funding Agreement is made as of \_\_\_\_\_, 2000, by and between Abbott Laboratories, ~~Inc.~~ <sup>LLC</sup>, an Illinois corporation ("~~Abbott~~", ("~~Abbott~~"), with its principal offices at 100 Abbott Park Road, Abbott Park, Illinois 60064-6049, and John Hancock Life Insurance Company, a Massachusetts corporation ("~~John~~" ("~~John Hancock~~"), ~~Hanecek~~"), with its principal offices at 200 Clarendon Street, Boston, Massachusetts 02117.

WITNESSETH

WHEREAS, Abbott is a global healthcare company actively engaged in the research and development of human pharmaceutical products;

WHEREAS, Abbott is interested in obtaining additional funding to support such research and development activities with respect to certain pharmaceutical products which are under development; and

WHEREAS, John Hancock is interested in providing such additional funding in exchange for the right to receive future milestone and royalty payments from Abbott.

NOW, THEREFORE, in consideration of the foregoing and the mutual covenants and undertakings contained herein, the parties hereto agree as follows:

ARTICLE I  
DEFINITIONS

In addition to the other terms defined elsewhere herein, the following terms shall have the following meanings when used in this Agreement (and any term defined in the singular shall have the same meaning when used in the plural and vice versa, unless stated otherwise):

1.1 "ABT-627" shall have the meaning given in Section 1.32.

1.11.2 "Affiliate" "Affiliate" shall mean, with respect to each party, any corporation or other form of business organization, which directly or indirectly owns, controls, is controlled by, or is under common control with, such party. An entity shall be regarded as being in control of another entity if the former entity has the direct or indirect power to order or cause the direction of the policies of the other entity whether (i) through the ownership of fifty percent (50%) or more in the United States, or thirty percent (30%) or more outside the United States, of the outstanding voting securities (or other ownership interest for a business organization other than a corporation) of that entity; or (ii) by contract, statute, regulation or otherwise.

1.21.3 "Aggregate" "Aggregate Carryover Amount" "Amount" shall have the meaning given in Section 3.3.

3466832.3

CONFIDENTIAL  
JH 004425



-2-

~~1.31.4~~ "Aggregate Spending Target" ~~"Target"~~ shall mean Six Hundred Twenty Million Dollars (\$620,000,000), such amount being the sum of the aggregate Program Payments to be made by John Hancock pursuant to Section 3.1 and the aggregate expenditures to be made by Abbott pursuant to Section 3.2.

~~1.41.5~~ "Annual Carryover Amount" ~~"Amount"~~ shall have the meaning given in Section 3.3.

1.6 "Annual Minimum Spending Target" for each Program Year shall mean the sum of (i) the Program Payment of John Hancock for such Program Year as specified in Section 3.1 (without giving effect to any deferral or other change under Section 3.3), (ii) Fifty Million Dollars (\$50,000,000), and (iii) any Annual Carryover Amount for such Program Year pursuant to Section 3.3.

~~1.51.7~~ "Annual Research Plan" ~~"Plan"~~ shall mean a reasonably and consistently detailed statement of Abbott's objectives, activities, timetable, FTE allocation and budget for its research and development activities related to the Program Compounds for every Program Year remaining in the Program Term. The Annual Research Plan for the first Program Year is attached as Exhibit 1.

~~1.6~~ "Annual Minimum Spending Target" for each Program Year shall mean the sum of (i) the Program Payment of John Hancock for such Program Year as specified in Section 3.1 (without giving effect to any deferral or other change under Section 3.3), (ii) Fifty Million Dollars (\$50,000,000), and (iii) any Annual Carryover Amount for such Program Year pursuant to Section 3.3.

~~1.71.8~~ "Bundled Product" ~~"Bundled Product"~~ shall have the meaning given in paragraph (b) of the definition of Net Sales.

~~1.81.9~~ "Combination Product" ~~"Combination Product"~~ shall mean any product containing one or more Program Compounds combined as a single pharmaceutical product with one or more other therapeutically active ingredients.

~~1.91.10~~ "Commercially Reasonable Efforts" ~~"Efforts"~~ [subject to discussion] shall mean efforts which are consistent with those normally used by other pharmaceutical companies with respect to other pharmaceutical products which are of comparable [potential] commercial value and market potential at a similar stage of development or product life, taking into account, without limitation, issues of safety and efficacy, product profile, proprietary status, the regulatory environment and the status of the product and other relevant scientific factors; ~~provided that, with respect to a particular Program Compound or Product, the existence of any other factors.~~

~~compound or product shall not be taken into account, including, without limitation, any compounds or products (i) in the marketplace or under development by Abbott or any other person, (ii) licensed (in licensed or otherwise), purchased or acquired by Abbott or its Affiliates, (iii) acquired by Abbott or its Affiliates as a result of any merger or of sale of equity or assets and (iv) in existence, in the marketplace, under development or licensed (in licensed or otherwise),~~

CONFIDENTIAL  
JH 004426

-3-

~~1.101.11~~ purchased or acquired by any person that acquires Abbott or its Affiliates as a result of any merger or of sale of equity or assets (and, as a result in any case, shall not reduce or otherwise change the efforts required of Abbott hereunder).

~~1.101.11~~ "Confidential Information" "Confidential Information" shall have the meaning given in Section 10.2.

~~1.111.12~~ "Delivery System Product" "Delivery System Product" shall have the meaning given in the definition of Net Sales.

~~1.121.13~~ "Dollars" or "\$" "Dollars" or "\$" means United States dollars.

~~1.131.14~~ "Eisai Agreement" "Eisai Agreement" shall mean the [agreement] dated June 29, 2000 between Eisai Co. Ltd. and Abbott related to the Program Compound "E7010" "E7010".

~~1.141.15~~ "Execution Date" "Execution Date" shall mean the date set forth in the introductory paragraph to this Agreement.

~~1.151.16~~ "FDA" "FDA" shall mean the U.S. Food and Drug Administration or any successor entity thereto.

~~1.16~~ "FTE" shall mean the time and work output equivalent to one year of a full time employee who is proficient in the performance of all assigned duties and responsibilities.

~~1.17~~ "First Commercial Sale" "Sale" shall mean the first sale of a Product in a given country by Abbott, its Affiliates or Licensees to an unrelated third person after Regulatory Approval has been granted in such country.

~~1.18~~ "Intellectual Property" "Intellectual Property" shall have the meaning given in Section 12.2.

~~1.19~~ "International Territory" "International Territory" shall mean all areas of the world outside the U.S. Territory (including Puerto Rico and the U.S. Virgin Islands).

~~1.20~~ "Investigational New Drug Application" "Investigational New Drug Application" shall have the meaning given in Section 6.3.

~~1.21~~ "Licensee" "Licensee" shall mean any party directly licensed by Abbott or its Affiliates to distribute or sell Products pursuant to a written license agreement on arm's-length terms and conditions.

~~1.22~~ "Losses" "Losses" shall mean any claims, demands, liabilities, costs, damages, judgments, settlements and other reasonable expenses (including attorneys' fees).

~~1.23~~ "NDA" "NDA" shall mean a New Drug Application filed with the FDA for the purpose of obtaining Regulatory Approval of a Product in the U.S. Territory.

CONFIDENTIAL  
JH 004427

-4-

1.24 ~~"Net Sales"~~ "Net Sales" shall mean:

- (a) the total gross sales of the Products (or, for purposes of clauses (b) and (c), the Bundled Products and Combination Products), in each case as set forth on the invoices for such sales by Abbott, its Affiliates and Licensees to ~~unrelated~~unaffiliated third parties in any given period, plus, if applicable, the fair market value of all properties and services received in consideration of a sale of Products, Bundled Products or Combination Products, as applicable, by Abbott, its Affiliates and Licensees to ~~unrelated~~unaffiliated third parties during such period, less the following deductions directly paid or actually incurred by Abbott, its Affiliates or Licensees during such period with respect to the sale of the Products, Bundled Products or Combination Products, as applicable, to the extent included in the gross invoiced sales price therefor:
  - (i) discounts, credits, rebates, allowances, adjustments, rejections, recalls and returns;
  - (ii) price reductions or rebates, retroactive or otherwise, imposed by government authorities;
  - (iii) sales, excise, turnover, inventory, value-added and similar taxes assessed on the royalty-bearing sale of Products;
  - (iv) transportation, importation, insurance and other handling expenses directly chargeable to the royalty-bearing sale of Products;
  - (v) charge backs granted to unaffiliated drug wholesalers; and
  - (vi) the portion of management fees paid to unaffiliated group purchasing organizations that relate specifically to the royalty-bearing sale of Products.
- (b) With respect to a Product which is sold together with any other products and/or services in a country at a unit price, whether packaged together or separately (a ~~"Bundled Product"~~, "Bundled Product"), the Net Sales of such Bundled Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Bundled Product shall be determined on a country-by-country basis as follows:
  - (i) multiply the Net Sales of such Bundled Product in such country by the fraction  $A/(A+B)$  where A is the average selling price of such Product in such country when sold separately and B is the total of the average selling prices in such country of each such other

CONFIDENTIAL  
JH 004428

-5-

product(s) and/or service(s) in such Bundled Product when sold separately; or

- (ii) if (x) either the average selling price of such Product or the total of the average selling prices of each such other products and/or services in such Bundled Product in such country is not available as of such date or (y) such Product is not sold separately in such country, multiply the Net Sales of such Bundled Product in such country by a percentage determined by the mutual agreement of the Parties which represents the proportionate economic value in such country of such Product relative to the economic value in such country contributed by the other products and/or services in such Bundled Product.
- (c) With respect to a Combination Product, the Net Sales of such Combination Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Combination Product shall be determined on a country-by-country basis as follows:
- (i) multiply the Net Sales of such Combination Product in such country by the fraction  $A/(A+B)$ , where A is the total of the average selling prices of the Program Compounds in such Combination Product, when sold separately in such country and B is the total of the average selling prices of each other therapeutically active ingredient when sold alone as a pharmaceutical product in such country; or
  - (ii) if (x) either the average selling price of all Program Compounds in such Combination Product or the total of the average selling prices of each other therapeutically active ingredient in such Combination Product in such country is not available or (y) such Program Compounds are not sold separately in such country, multiply the Net Sales of such Combination Product by a percentage determined by mutual agreement of the Parties, which represents the proportionate economic value in such country of all Program Compounds in such Combination Product relative to the economic value in such country contributed by all other therapeutically active ingredients in such Combination Product.
- (d) For purposes of this paragraph (d), a "~~Premium~~ Premium Delivery System" ~~System~~ means any delivery system comprising device(s), equipment, instrumentation or other components (but not solely containers or packaging) designed to assist in the administration of a Product[, such as the Abbott ADD-Vantage® System]. With respect to a Product which is sold together with a Premium Delivery System (a "~~Delivery System Product~~" Delivery System Product) in a country at a unit price, the Net

CONFIDENTIAL  
JH 004429

-6-

Sales of such Delivery System Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Product shall be determined on a country-by-country basis as follows:

- (i) if the Product is sold separately without the Premium Delivery System in a country, reduce the Net Sales of such Delivery System Product in such country by the amount that the average selling price of the Delivery System Product in such country exceeds the average selling price of such Product as sold separately in such country; or
  - (ii) if the Product is not sold separately without the Premium Delivery System in such country, reduce Net Sales of such Delivery System Product by an amount, determined by mutual agreement of the Parties, which represents the proportionate economic value in such country added by the Premium Delivery System.
- (e) With respect to EndothelinCompound ABT-627 [define], if EndothelinCompound ABT-627 is developed and marketed by Abbott for one or more cancer indications and one or more non-cancer indications, Net Sales shall be based upon sales of Product only for the cancer indication(s). If the Product is sold with different dosage strengths for the cancer indications and non-cancer indications, Net Sales shall be calculated based on the sales of the dosage strength(s) which are approved by the FDA for the treatment of cancer. If any dosage strength is the same for one or more cancer indications and one or more non-cancer indications, the Parties shall mutually agree to a formula, based upon IMS [define] or other market research data, that allocates the sales of such dosage strength between the cancer indication(s), which would be included as part of Net Sales, and the non-cancer indication(s) which would be excluded from Net Sales.

1.25 "~~Neutral~~" "Neutral" shall have the meaning given in Section 11.2-Exhibit 16.7.

1.26 "~~Parties~~" "Parties" shall mean Abbott and John Hancock.

1.27 "~~Phase I Clinical Trial~~" "Trial" shall mean those clinical trials which utilize a limited number of human beings to preliminarily address safety and to determine what doses can be safely tolerated.

1.28 "~~Phase II Clinical Trial~~" "Trial" shall mean those controlled clinical trials, the primary objective of which is to ascertain additional data regarding the safety and tolerance of one of the Program Compounds and preliminary data regarding such Program Compound's efficacy.

**CONFIDENTIAL**  
JH 004430

-7-

1.29 ~~"Phase III Clinical Trial"~~"Trial" shall mean one or a series of controlled pivotal studies of a specific Product by administration of such Product to human beings where the principal purpose of such trial is to provide confirmatory safety and efficacy data necessary to support the filing for Regulatory Approval of a Product.

1.30 ~~"Premium Delivery System"~~"System" shall have the meaning given in paragraph (d) of the definition of Net Sales.

1.31 ~~"Product"~~"Product" shall mean any product containing one or more of the Program Compounds as an active ingredient, alone or in combination with other active ingredients (including any Bundled Product and any Combination Product).

1.32 ~~"Program Compounds"~~"Program Compounds" shall mean the preclinical, Phase I, Phase II, and Phase III compounds listed on ~~Exhibit 1.32~~, as well as any substitute back-up compounds added by Section 4.3, and any line extensions, any new formulations, all indications and any improvements, derivatives and modifications thereof; provided, however, that with respect to ~~Endothelin Compound ABT-627~~ (hereinafter, "Compound ABT-627"), it shall only be considered a Program Compound to the extent that it is used to treat cancer.

1.33 ~~"Program Inventions"~~"Program Inventions" shall have the meaning given in Section 5.1.

1.34 ~~"Program Payments"~~"Program Payments" shall have the meaning given in Section 3.1.

1.35 ~~"Program Related Costs"~~ shall mean all direct ~~and indirect~~ "Program Related Costs" shall mean (i) all direct and indirect costs and expenses that are ~~spent~~ incurred by Abbott on the Research Program during a given Program Year; (ii) ~~any payments made by Abbott to John Hancock pursuant to Sections 6.1, 6.2 and 6.3(a) through (e); and (iii) the milestone and license fees paid by Abbott to Eisai Co. Ltd. with respect to the Program Compound "E7010" pursuant to the Eisai Agreement.~~ In no event shall (a) any payments made by Abbott to John Hancock pursuant hereto or (b) any overhead or similar charges or expenses, to Section 6.3(f) constitute Program Related Costs. Exhibit 1.35 is an example of Program Related Costs for a Program Compound.

1.36 ~~"Program Term"~~"Program Term" shall mean a period of four ~~(4)~~ consecutive (4) Program Years.

1.37 ~~"Program Year"~~"Program Year" shall mean a period of twelve (12) consecutive calendar months, with the first Program Year commencing on \_\_\_\_\_, 2000 and each subsequent Program Year commencing on the anniversary of such date.

1.38 ~~"Quarterly Reporting Period"~~"Period" shall mean the calendar quarter with respect to the U.S. Territory and a fiscal quarter ending on the final day of February, May, August and November (as the case may be) for the International Territory; provided, however, that if Abbott adopts the calendar year as its fiscal year for the International Territory, then the Quarterly Reporting Period for the International Territory shall also be the calendar quarter.

CONFIDENTIAL  
JH 004431



-8-

1.39 ~~"Research Program"~~ "Research Program" shall mean all of Abbott's, its Affiliates and Subcontractors' activities directed towards obtaining Regulatory Approval for the Products, including research, development, safety and efficacy studies, clinical trials, process development, formulation work, regulatory, quality, data collection and analysis and project management.

1.40 ~~"Regulatory Approval" shall mean:~~ (i) with "Regulatory Approval" shall mean: (i) with respect to the U.S. Territory, the receipt of approval from the FDA to market a Product in the U.S. Territory; and (ii) with respect to any country in the International Territory, receipt of the governmental approvals required to market a Product in such country, including any pricing and reimbursement authorization required in such country.

1.41 ~~"Royalty Term"~~ "Royalty Term" shall mean, with respect to each Product in each country, a period of ten (10) years from the date of First Commercial Sale of such Product in such country.

1.42 ~~"Subcontractor"~~ "Subcontractor" shall have the meaning given in Section 2.4.

1.43 ~~"Territory"~~ "Territory" shall mean both the U.S. Territory and the International Territory.

1.44 ~~"U.S. Territory"~~ "U.S. Territory" shall mean the United States of America, excluding Puerto Rico and the U.S. Virgin Islands.

## ARTICLE 2 ANNUAL RESEARCH PROGRAM

2.1 Program Term. The Research Program shall be conducted by Abbott during the Program Term, and beyond the Program Term until Abbott either abandons development in accordance with the terms hereof or receives Regulatory Approval for each Program Compound.

2.2 Research Plan. The Research Program shall be conducted by Abbott in each Program Year in accordance with the Annual Research Plan for such Program Year. The Annual Research Plan will be provided to John Hancock until Abbott either abandons development in accordance with the terms hereof or receives Regulatory Approval for each Program Compound in the U.S. Territory. The Annual Research Plan shall be prepared by Abbott and presented to John Hancock at least sixty (60) days prior to the start of each Program Year. The Annual Research Plan for the first Program Year is attached as Exhibit 1. Abbott may modify the Annual Research Plan from time to time in order to best meet the objectives of the Research Program. Any such modifications to the Annual Research Plan shall be promptly provided to John Hancock.

2.3 Conduct of Research. Abbott shall use Commercially Reasonable Efforts to conduct the Research Program in good scientific manner and using good laboratory practices, to achieve the objectives of the Research Program efficiently and expeditiously and to comply with all applicable laws and regulations. Notwithstanding anything in this Agreement to the contrary,

CONFIDENTIAL  
JH 004432

-9-

Abbott does not represent, warrant or guarantee that the Research Program will be successful in whole or in part or result in the registration or commercialization of any pharmaceutical products or that any Products obtaining Regulatory Approval will be a commercial success.

2.4 Subcontracting Research. Abbott may subcontract or outsource to Affiliates or third persons (each, a "~~Subcontractor~~" "Subcontractor") any portion of the Annual Research Plan. Each non-affiliated Subcontractor shall enter into a confidentiality agreement with Abbott and agreements acknowledging Abbott's exclusive ownership of the Program Compounds and shall comply with the terms hereof and with all applicable laws and regulations, including good laboratory practices, with respect to its work on the Research Program. Abbott shall supervise and be responsible under this Agreement for the work of such Subcontractor on the Research Program and no subcontracting or outsourcing shall relieve Abbott of any of its obligations hereunder.

2.5 Research Reports and Records. Abbott shall on an annual basis [no later than the last day of each Program Year]~~[This report must be provided before John Hancock can be obligated under section 3 to make a subsequent Program Payment]~~; provide John Hancock with a reasonably detailed report setting forth the status of the Research Program and all Program Related Costs expended by Abbott during such Program Year. Such report shall also contain such other information related thereto as John Hancock may reasonably request from time to time. Abbott shall, and shall cause each Subcontractor to, maintain complete and accurate records, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes and for purposes of demonstrating compliance with the terms hereof, that fully and properly reflect all work done, results achieved and Program Related Costs expended in performance of the Research Program. The books and records of Abbott and each Subcontractor related to the Research Program, including, without limitation, those related to the expenditure of Program Related Costs, shall be subject to copying, inspection and audit by (and at the expense of) John Hancock at any time and from time to time. Such audit shall occur upon reasonable notice and during normal business hours by an independent auditor selected by John Hancock and reasonably acceptable to Abbott. John Hancock and its independent auditor shall maintain such records and information of Abbott in confidence in accordance with Article 10 and shall not use such records or information except to the extent permitted by this Agreement, including any enforcement of the provisions hereof. In the event that such audit reveals any material breach of Abbott's responsibilities hereunder, Abbott shall (i) pay the reasonable fees and expenses charged by such auditor, and (ii) fully and promptly cure such breach ~~and (iii) all documents reviewed in the audit will be copied and delivered to John Hancock at its request.~~

### ARTICLE 3 RESEARCH FUNDING

3.1 John Hancock Program Payments. John Hancock shall make the following installment payments for the applicable Program Year to Abbott to help support the Research Program (the "~~Program Payments~~" "Program Payments"):

CONFIDENTIAL  
JH 004433



-10-

<u>Payment Date</u>	<u>Payment Amount</u>	<u>Program Year</u>
Execution Date	\$50,000,000	first
First Anniversary of Execution Date	\$55,000,000	second
Second Anniversary of Execution Date	\$55,000,000	third
Third Anniversary of Execution Date	\$60,000,000	fourth

Such funds shall be expended by Abbott on Program Related Costs and not for any other purpose.

3.2 Abbott Program Payments. Abbott shall spend on Program Related Costs: (i) ~~at (i) during each Program Year, at least the Annual Minimum Spending Target for and during each such Program Year and (ii) at (ii) at least the Aggregate Minimum Spending Target for and during the Program Term.~~ John Hancock's sole and exclusive remedies for Abbott's failure to fund the Research Program in accordance with this Section 3.2 (but not for any other breach of Abbott's other obligations) are set forth in Sections 3.3, 3.4 and 7.2.3.3 and 3.4.

3.3 Carryover Provisions. Abbott shall be permitted to change its funding obligations under Section 3.2 only as follows:

- (i) If in any Program Year Abbott spends on Program Related Costs, the full amount of the Program Payment provided by John Hancock for such Program Year, but does not spend the full amount of the Annual Minimum Spending Target for such Program Year (including any Annual Carryover Amounts from any prior Program Years), Abbott will spend the difference between its expenditure on Program Related Costs for such Program Year and the Annual Minimum Spending Target for such Program Year (the ~~"Annual"~~ "Annual Carryover Amount" Amount) in the subsequent Program Year. John Hancock's obligation to make any Program Payment for such subsequent Program Year, if any, pursuant to Section 3.1, shall be deferred until the time that Abbott notifies John Hancock that it has spent the Annual Carryover Amount in such subsequent Program Year; and
- (ii) If ~~in for~~ each Program Year Abbott spends on Program Related Costs at least the Annual Minimum Spending Target, with or without utilizing the carryover permitted in paragraph (i), but does not expend the full amount of the Aggregate Spending Target during the Program Term, Abbott will expend the difference between its expenditures for Program Related Costs during the Program Term and the Aggregate Spending Target (the ~~"Aggregate"~~ "Aggregate Carryover Amount" Amount) on Program Related Costs during the subsequent fiscal year commencing immediately after the end of the Program Term. If Abbott does not spend the Aggregate Carryover Amount on Program Related Costs during such subsequent fiscal year, Abbott will refund to John Hancock one-third of the Aggregate Carryover Amount that remains unspent by Abbott, within thirty (30) days of the end of such subsequent fiscal year.

CONFIDENTIAL  
JH 004434

-11-

3.4 Termination of John Hancock's Program Payment Obligation. If Abbott: ~~(i) abandons~~(i) abandons development of all Program Compounds during the Program Term; ~~(ii) does~~(ii) does not expend during any Program Year the full amount of the Program Payment provided~~made~~ by John Hancock for such Program Year; ~~(iii) fails to timely deliver its Annual Research Plan for any year in accordance with Section 2.2 or does not reasonably demonstrate in its Annual Research Plan, its intent and reasonable expectation to expend Program Related Costs during the next Program Year in excess of the Program Payment provided by John Hancock for such year; or~~ (iv) ~~does~~(iv) does not reasonably demonstrate, in its Annual Research Plan, its intent and reasonable expectation to expend Program Related Costs during the Research Term in excess of the Aggregate Spending Target, John Hancock's obligation to make any remaining Program Payments pursuant to Section 3.1 shall cease. In addition, in the case of either (i) or (ii) above, Abbott shall refund (not later than the 10th day following such event) to John Hancock the amount, if any, by which the Program Payment for such year minus half made by John Hancock for such year, if any, exceeds one-half of the Program Related Costs actually spent by Abbott during that Program Year.

3.5 Hancock Funding Obligation. John Hancock's entire obligation hereunder shall be limited to providing the Program Payments set forth in Section 3.1. Abbott shall be solely responsible for funding all Program Related Costs in excess of the Program Payments from John Hancock.

~~3.6 Calculation of Expenditures. Notwithstanding anything else in this Agreement, for purposes of calculating whether Abbott has spent, or is projected to have spent, Program Related Costs in excess of (i) the Annual Minimum Spending Target for the first Program Year and (ii) the Aggregate Spending Target for the Program Term, Abbott shall be entitled to include within such calculations all cost and expenses incurred on or after [ ], 2000 up to the Execution Date, which would have otherwise qualified as Program Related Costs in the event that the period from [ ], 2000 to the Execution Date had been included within the first Program Year (and the Program Term). This extension of the first Program Year for the determination of whether the Annual Minimum Spending Target for the first Program Year and the Aggregate Spending Target are met, takes into consideration that Abbott was funding all research and development cost for the Program Compounds commencing [ ], 2000.~~

#### ARTICLE 4 PRODUCT RESEARCH AND DEVELOPMENT

4.1 Commercially Reasonable Efforts. Abbott shall be solely responsible for the clinical development, government approval, manufacturing, marketing, sales and distribution of Products. Abbott will use, and will cause each of its Affiliates and Licensees to use, Commercially Reasonable Efforts to pursue the clinical development, government approval, manufacturing, marketing, sales and distribution of Products throughout the Territory. The obligations of Abbott, its Affiliates and Licensees with respect to any Product under this Article 4 are expressly conditioned upon the safety, efficacy and commercial feasibility of each Product, but no license, assignment or other transfer of rights by Abbott (by operation of Article 14 or otherwise) will modify or reduce Abbott's obligations hereunder. [It is the parties' expectation that under normal circumstances]~~[addressed by proviso at end of sentence?]~~ Abbott will file for

CONFIDENTIAL  
JH 004435

-12-

Regulatory Approval with respect to each Product in Europe within two (2) years from the date of the NDA filing for such Product in the U.S. Territory and in Japan within five (5) years from such NDA filing date; provided, however, that these time frames may be extended or otherwise altered based upon unforeseen circumstances that legitimately impact such regulatory filings in such foreign jurisdictions.

4.2 Marketing and Sale Responsibility. Without limiting the generality of Section 4.1, within six (6) months of obtaining Regulatory Approval for a Product in a given country, Abbott, its Affiliates or Licensees shall commence to market and sell such Product in such country. Abbott's obligation to market and sell a Product shall not apply [Why doesn't "Commercially Reasonable Efforts" address all of this?] to a Product in any country if Abbott has not commenced or has ceased marketing and selling such Product in such country substantially/primarily on account of adverse business or financial conditions caused by the regulatory authorities or other governmental authorities of such country (including not commencing marketing and selling in a country where the regulatory authorities have price or reimbursement approval and the price or reimbursement approval [or that proposed by the regulatory authorities or government authorities] is unacceptable to Abbott) which causes the marketing and sale of such Product in such country to be contrary to the financial best interests of John Hancock and Abbott; provided, however, that Abbott, its Affiliates or Licensees shall commence or resume marketing and sale of such Product in such country as soon as reasonably practical after such adverse business or financial conditions cease to exist.

4.3 Alternative Compounds. ~~[subject to discussion]~~ In the event that Abbott

- (a) ~~divests or out licenses a Program Compound (which shall mean a sale, license or other transfer by Abbott following which Abbott and its Affiliates no longer have the exclusive right in (i) North America or (ii) at least two thirds (by population) of Japan and Western Europe (consisting of [the European Union]), to [develop and sell] any Product containing such Program Compound); or~~
- (b) ~~fails or ceases to research, develop, market, distribute or sell any Program Compound or Product for any reason that is not clearly consistent with using its Commercially Reasonable Efforts; or~~
- (c) ~~fails or ceases to develop any Program Compound beyond a preclinical or Phase I Clinical Trial,~~

Abbott shall give John Hancock a choice among three (3) alternative compounds as a substitute for such Program Compound (and, in the case of subsection (a) above, John Hancock shall additionally have the alternative choice of retaining its rights hereunder with respect to such Program Compound), provided that John Hancock reasonably agrees that at least two (2) of the alternative compounds then have a similar market opportunity and are in a comparable stage of development or have a better development and risk profile than such Program Compound. Upon selection by John Hancock, such selected alternative compound shall thereafter be treated hereunder as a Program Compound (including applicability of the representations and warranties herein with respect thereto as of the date it is added to the Research Program), but such selection

CONFIDENTIAL  
JH 004436

-13-

will not occur unless John Hancock notifies Abbott of its selection of one of the alternative compounds (or of retaining its rights with respect to the Program Compound) within thirty (30) days from the date that Abbott proposes the alternative compounds to John Hancock and provides John Hancock with information about such alternative compounds of the same scope as that provided to John Hancock with respect to the initial Program Compounds and such additional information as John Hancock may reasonably request. In addition, such thirty (30) day period shall be extendable by another forty five (45) days by written notice to such effect from John Hancock to Abbott within such initial thirty (30) day period.

If, in the case of subsection (a) above, John Hancock elects to retain its rights hereunder with respect to a Program Compound that has been divested or out licensed, Abbott shall cause the transferee thereof to acknowledge and agree to the terms of this Agreement as applied to such Program Compound pursuant to such agreements and other instruments as are reasonable acceptable to John Hancock.

In addition, whether or not John Hancock elects to retain its rights with respect to a Program Compound, in the event that Abbott divests or out licenses such Program Compound under the circumstances described in subsection (a) above, any initial or lump sum payment received by Abbott or its Affiliates with respect thereto shall be added to and included in the Net Sales as of the date such payment is due and payable to Abbott.

4.4. Endothelin. With respect to Endothelin, if Abbott, its Affiliates or Subcontractors initiates a Phase [III] Clinical Trial for one or more non-cancer indications [within \_\_\_\_\_ years from the date of this Agreement], Abbott will provide notice thereof to John Hancock together with information similar to that which John Hancock received in connection with the Program Compounds hereunder. Abbott will provide additional information concerning Endothelin and such trial as reasonably requested by John Hancock. Abbott agrees to give John Hancock the option, exercisable in John Hancock's sole discretion, to provide approximately \_\_\_\_\_ % of the additional research funding required with respect to Endothelin for all non-cancer indications (not to exceed \$ \_\_\_\_\_), on terms and conditions that will (i) provide a projected rate of return to John Hancock that is at least as good as the projected rate of return provided herein with respect to the Program Compounds as of the date hereof and (ii) be negotiated in good faith by the Parties. Unless John Hancock shall have notified Abbott of its exercise of such option, such option will expire [\_\_\_\_\_] months after John Hancock receives the information requested by it as described above. Failure of Program Compound to Progress. If a Program Compound fails to progress past Phase I Clinical Trial (i.e., does not enter a Phase II Clinical Trial) (a "Failed Program Compound"), and Abbott initiates the development of a back-up compound, including any in-licensed back-up compound in the same class of compounds with the same mechanism of action for the same indications as the Failed Program Compound, during the Program Term or any period immediately thereafter during which the Aggregate Carryover Amount is being spent, then such back-up compound shall be deemed a Program Compound. With respect to any Failed Program Compound for which Abbott does not initiate development of a back-up compound as set forth above, then Abbott shall have no further obligations to John Hancock with respect to such Failed Program Compound. With respect to any Program Compound which enters a Phase II Clinical Trial but which Abbott thereafter ceases the development of, John Hancock shall have no further rights with respect to such Program Compound or any other back-up compound or in-licensed back-up compound developed by Abbott.

CONFIDENTIAL  
JH 004437



-14-

4.4. Compound ABT-627. With respect to Compound ABT-627, if Abbott, its Affiliates or Subcontractors initiates a Phase [II] Clinical Trial for one or more non-cancer indications during the Program Term or any period immediately thereafter during which the Aggregate Carryover Amount is being spent, Abbott will provide notice thereof to John Hancock together with information similar to that which John Hancock received in connection with the Program Compounds hereunder. Abbott will provide additional information concerning Compound ABT-627 and such trial as reasonably requested by John Hancock. Abbott agrees to give John Hancock the option, exercisable in John Hancock's sole discretion, to provide approximately 33 1/3% of the additional research funding required with respect to Compound ABT-627 for all non-cancer indications. John Hancock shall have forty-five (45) days from Abbott's notice to notify Abbott of its interest. If John Hancock has not notified Abbott with in such forty-five (45) day period, the option shall be deemed expired. If John Hancock participates in such funding, Net Sales of Products shall include Net Sales generated by sales of Compound ABT-627 for such additional indication(s) upon Abbott's receipt of FDA approval for such indication(s).

4.5. Arm's-Length. Abbott shall not research, develop, manufacture, market, sell, distribute, out-license or otherwise treat any Program Compounds or Products differently, as compared to any other Abbott compounds or products, on account of any of John Hancock's rights hereunder. Furthermore, all distribution agreements, licenses, out-licenses and other agreements relating to the research, development, manufacturing, marketing, sale, distribution, licensing, out-licensing or divestiture of and all other transactions involving any Program Compounds or Products to or with any third party (except to Abbott's Affiliates) shall be on arm's-length terms and conditions.

## ARTICLE 5 PROGRAM INVENTIONS

5.1. Ownership. All inventions, innovations, ideas, discoveries, technology, know-how, methods, data, applications and products (in each case whether or not patentable) arising from the Research Program or otherwise related to the Program Compounds (collectively, the "Program" "Program Inventions" "Inventions") shall be exclusively owned by or assigned to Abbott and Abbott shall not divest or otherwise transfer any right, title or interest in or to any Program Inventions to any other person except in accordance with Sections 4.3 and 4.5, which would prevent or impair Abbott's ability to fulfill its obligations to John Hancock under this Agreement.

5.2. Patent Prosecution and Maintenance. Abbott will use Commercially Reasonable Efforts to obtain broad patent protection for the Program Inventions. Abbott shall be responsible for all costs and expenses and control all decisions related to filing for patent protection, including the preparation, filing (foreign and/or domestic), prosecution, issuance and maintenance of patent applications or patents covering Program Inventions.

5.3. Enforcement. Abbott shall have the sole right and authority to enforce the patents or any other rights arising from Program Inventions against any infringers. If Abbott initiates any

CONFIDENTIAL  
JH 004438

-15-

action or lawsuit to enforce such patents or other rights, it shall be solely responsible for the cost and expense thereof. Abbott will promptly notify John Hancock at such time as it becomes aware of any infringement activities and of any such enforcement actions or lawsuit, and Abbott will provide information concerning them as reasonably requested by John Hancock. All moneys recovered upon the final judgment or settlement of any such action or lawsuit, ~~less the out-of-pocket cost and expense thereof~~, shall be added to and included in the Net Sales (for the years in each Royalty Term with respect to which such action or lawsuit concerns), ~~less the out-of-pocket cost and expense concerns~~; thereof, provided that if such recovered moneys represent something other than Net Sales by the infringer (e.g., lost profits or a royalty), Abbott agrees to allocate a portion of the recovered moneys to John Hancock so as to approximate the appropriate royalty on Net Sales by the infringer during each year of the Royalty Terms. [Unclear on the intent of this provision?]

#### ARTICLE 6 MILESTONE PAYMENTS TO JOHN HANCOCK

6.1 Closing Fee. Upon execution of this Agreement, Abbott shall pay \_\_\_\_\_ (\$\_\_\_\_\_) to John Hancock. Any payment here will exceed \$20 million?

6.2 Management Fee. On \_\_\_\_\_ 2001, 2002, 2003 and 2004, Abbott shall pay to John Hancock a management fee, each of which shall be in the amount of Two Million Dollars (\$2,000,000).

6.3 Milestone Notification and Payments. Abbott shall promptly notify John Hancock of the occurrence any of the following events that give rise to Abbott's obligation to make a milestone payment. Except as hereinafter limited, Abbott shall pay the following milestone payments to John Hancock in the amounts and at the times set forth below with respect to each Program Compound:

- (a) One Million Dollars (\$1,000,000) shall be paid within thirty (30) days after the allowance by the FDA of the first Investigational New Drug Application [define] for such Program Compound;
- (b) Two Million Dollars (\$2,000,000) shall be paid within thirty (30) days after the initiation of the first Phase I Clinical Trial with such Program Compound;
- (c) Three Million Dollars (\$3,000,000) shall be paid within thirty (30) days after the initiation of the first Phase II Clinical Trial with such Program Compound;
- (d) Four Million Dollars (\$4,000,000) shall be paid within thirty (30) days after the initiation of the first Phase III Clinical Trial with such Program Compound;

CONFIDENTIAL  
JH 004439

-16-

- (e) Five Million Dollars (\$5,000,000) shall be paid within thirty (30) days after the filing of ~~an~~the first NDA with the FDA for such Program Compound; and
- (f) Ten Million Dollars (\$10,000,000) shall be paid within thirty (30) days after the first Regulatory Approval of such Program Compound in the U.S. Territory.

The aggregate of milestone payments under Section 6.3(a), (b), (c), (d), and (e) for all Program Compounds shall be limited to Twelve Million Dollars (\$12,000,000), and once such aggregate limit has been paid, no further payments shall be due and payable under Sections 6.3(a), (b), (c), (d) or (e). The aggregate of milestone payments under Section 6.3(f) for all Program Compounds shall be limited to Forty Million Dollars (\$40,000,000), and once such aggregate limit has been paid, no further payments shall be due and payable under Section 6.3(f). The aggregate of milestone payments under Sections 6.3(a), (b), (c), (d) and (e) for all Program Compounds shall be limited to Three Million Dollars (\$3,000,000) during the first Program Year and shall be limited to Six Million Dollars (\$6,000,000) during the second Program Year, and once such annual limit has been reached for these particular Program Years, no further payments shall be due under Sections 6.3(a), (b), (c), (d) and (e) for the remainder of such Program Year; provided that any amounts that would have been due to John Hancock but for such annual limits shall be paid in subsequent Program Years so long as the Program Compound to which it relates has not been abandoned, divested or out-licensed by Abbott. Further, the milestone payments set forth in Section 6.2 will not be made more than once with respect to any given Program Compound regardless of the number of such trials, filings or approvals that may be undertaken or granted with respect to such Program Compound, including, without limitation, multiple product forms of the same Program Compounds, additional active or inactive ingredients, indications, delivery modules and/or dosage strengths. Finally, a milestone payment shall only be made with respect to a milestone achieved after [ ], ~~2000~~the date of this Agreement. For instance, if a Program Compound is in Phase III Clinical Trials at the Effective Date on [ ], ~~2000~~of this Agreement, then no milestones shall ever be paid under Sections 6.3(a), (b), (c) and (d) for such Program Compound regardless of whether the Program Compound were ever to achieve such milestones as part of a different development program for instance for a new dosage strength or new indication. Exhibit 6. — 6.3 sets forth the current stage of clinical development for each Program Compound.

## ARTICLE 7 ROYALTIES

7.1 Royalty Rates. Subject to the limitation set forth below, Abbott shall pay to John Hancock royalties equal to the following percentages calculated on a calendar year to calendar year basis on the aggregate Net Sales of all Products in the Territory:

CONFIDENTIAL  
JH 004440



-17-

<u>Royalty percentage</u>	<u>Calendar year Net Sales (in millions) of all Products in the Territory</u>
8% of those Net Sales	up to \$400
and then 4% of those Net Sales	in excess of \$400 up to \$1,000
and then 1% of those Net Sales	in excess of \$1,000 up to \$2,000
and then .5% of those Net Sales	in excess of \$2,000

7.2 Royalty Term. The obligation to make royalty payments on each Product shall be calculated on a country-by-country basis, shall commence for such Product upon the First Commercial Sale thereof in such country, and shall last for the duration of the Royalty Term in each given country for such Product. Notwithstanding anything to the contrary herein, the obligation to make royalty payments on the Products shall not begin until [\_\_\_\_\_, 2002] [the commencement of the Third Program Year] (and with respect only to Net Sales occurring on or after such date) and shall cease at December 31, 2014; provided that (i) for each Annual Carryover Amount that exceeds \$\_\_\_\_\_, the obligation to make royalty payments shall be extended by one additional year and (ii) if Abbott becomes obligated to pay an Aggregate Carryover Amount pursuant to Section 3.3(ii) in an aggregate amount in excess of \$\_\_\_\_\_, the obligation to make royalty payments shall also be extended by one additional year.

## ARTICLE 8 ROYALTY REPORTS AND ACCOUNTING

8.1 Reports, Exchange Rates. With respect to every Quarterly Reporting Period for which Abbott is obligated to pay a royalty hereunder, Abbott shall furnish to John Hancock a written report for such Quarterly Reporting Period within sixty (60) days of the end of such Quarterly Reporting Period [(that is, within sixty (60) days of each [March 31], [June 30], [September 30] and [December 31])] showing in reasonably specific detail:

- (a) the total gross sales in each country for each Product sold by Abbott, its Affiliates and Licensees in the Territory and the detailed calculation of Net Sales from gross sales in each country for each Product;
- (b) the royalties payable in Dollars, if any, which shall have accrued hereunder;
- (c) the dates of the First Commercial Sale of the Product in any country in the Territory during such Quarterly Reporting Period;
- (d) the exchange rates used in determining the amount of Dollars.
- (e) [WITHHOLDING TAXES DELETED HERE - WHY?]

With respect to sales of Products invoiced in Dollars, the gross sales, Net Sales (including all adjustments and deductions permitted to be made hereunder in calculating the same), and royalties payable shall be expressed in Dollars. With respect to sales of Products invoiced in a

CONFIDENTIAL  
JH 004441

-18-

currency other than Dollars, the gross sales, Net Sales and royalties payable shall be expressed in their Dollar equivalent, calculated [using the Inter Bank rate set forth in the International Report published by International Reports Inc. as Foreign Exchange Rates quoted in New York on the day nearest the last business day of] [or the weighted average exchange rate on each day during ?] the Quarterly Reporting Period. [The gross sales made outside the U.S. Territory during a fiscal quarter will be reported with the gross sales made in the U.S. Territory during the calendar quarter in which the last month of the fiscal quarter falls.]

## 8.2 Audits.

- (a) Upon the written request of John Hancock and, in the absence of any breach by Abbott hereunder, not more than once in each calendar year, Abbott shall permit John Hancock and an independent certified public accounting firm of nationally recognized standing, selected by John Hancock and reasonably acceptable to Abbott, at John Hancock's expense, to have access during normal business hours to such of the records of Abbott, its Affiliates and Licensees to verify the accuracy of the royalty reports and the amounts and calculation of any payments required hereunder for any year ending not more than thirty-six (36) months prior to the date of such request; provided that, if such access reveals that any additional royalties or other payments were owed during such period, John Hancock shall have access to all such records for any year.
- (b) If such accounting firm concludes that additional royalties or other payments were owed during such period, Abbott shall have the option to invoke the proceedings of Section 16.7 below or pay the additional royalties or other payments within thirty (30) days of the date John Hancock delivers to Abbott such accounting firm's written report so concluding. The reasonable fees and expenses charged by such accounting firm shall be paid by John Hancock; provided, however, if the audit discloses that the amounts payable by Abbott for any Quarterly Reporting Period are more than one hundred five percent (105%) of the royalties actually paid for such period, then Abbott shall pay the reasonable fees and expenses charged by such accounting firm and any related costs of enforcement.
- (c) Abbott shall include in each license granted by it pursuant to this Agreement a provision requiring the Licensee (including any Affiliates of Abbott) to make reports to Abbott, to keep and maintain records of Net Sales made pursuant to such license and to grant access to such records by John Hancock and its accounting firm or other auditor to the same extent required of Abbott under this Agreement.
- (d) In the event that Abbott's document retention policy requires it to discard any documentation related to the Research Program, Program Compounds or Net Sales (which policy shall require documents to be retained for at least three (3) years), prior to discarding such documentation Abbott shall

CONFIDENTIAL  
JH 004442

-19-

~~make it~~ All reports and payments not disputed as to correctness by John Hancock within three (3) years after receipt thereof shall thereafter conclusively be deemed correct for all purposes, and Abbott and its Affiliates and licensees shall be released from any liability or accountability with respect to such royalties available to John Hancock for John Hancock's direct retention or copying and payments.

8.3 **Confidential Financial Information.** John Hancock shall treat all information subject to review under this Article 8, and shall cause its accounting firm to agree to treat all such information, in accordance with the provisions of Article 10.

8.4 **Accounting Principles.** All accounting hereunder, including without limitation all determinations of gross sales, Net Sales (including all adjustments and deductions permitted to be made hereunder in calculating the same), Program Related Costs and all calculations underlying such determinations, shall be made in accordance with generally accepted accounting principles as in effect in the United States, consistently applied.

## ARTICLE 9 PAYMENTS

9.1 **Payment Terms.** With respect to every Quarterly Reporting Period for which Abbott is obligated to pay a royalty hereunder, such royalties shall be due and payable within sixty (60) days of the end of such Quarterly Reporting Period [(that is, within sixty (60) days of each [March 31], [June 30], [September 30] and [December 31])]. Payment of royalties in whole or in part may be made in advance of such due date.

9.2 **Payment Method.** All royalties and other payments by Abbott to John Hancock under this Agreement shall be made by bank wire transfer in immediately available funds in accordance with the instructions set forth on Exhibit 9.2 attached hereto or in accordance with such other instructions as John Hancock may give from time to time.

9.3 **Withholding Taxes [TAX].** All amounts owing from Abbott to John Hancock under this Agreement shall be paid without deduction to account for any withholding taxes, value-added taxes or other taxes, levies or charges with respect to such amounts payable on behalf of Abbott, its Affiliates or Licensees and any taxes required to be withheld on behalf of Abbott, its Affiliates or Licensees in any country within the Territory.

9.4 **Late Payments.** Abbott shall pay interest to John Hancock on the aggregate amount of any payments by Abbott that are not paid on or before the date such payments are due under this Agreement, including, without limitation, any disputed payments or payments resulting from any audit, at a rate per annum equal to the lesser of (a) the prime rate of interest plus \_\_\_\_ basis points as reported by \_\_\_\_ bank in \_\_\_\_, from time to time (with any change in such reported rate being effective immediately for purposes hereof), or (b) the highest rate permitted by applicable law, calculated on the number of days such payments is delinquent until paid in full in cash. All such amounts shall be payable upon demand.

CONFIDENTIAL  
JH 004443

-20-

## ARTICLE 10 CONFIDENTIALITY

10.1 Nondisclosure Obligations. Except as otherwise provided in this Article 10, during the term of the Agreement and for a period of ten (10) years thereafter, (a) John Hancock shall maintain in confidence in accordance with such procedures as are adopted by John Hancock to protect its own confidential information of third parties delivered to it, and shall use only for purposes of this Agreement (including, without limitation, enforcement of the terms hereof), information and data related to the Program Compounds or Products; and (b) John Hancock shall also maintain in confidence in accordance with such policies, and use only for purposes of this Agreement, all information and data supplied by Abbott under this Agreement, which if disclosed in writing is marked "~~confidential~~", "~~confidential~~", if disclosed orally is promptly thereafter summarized and confirmed in writing to the other party and marked "~~confidential~~", "~~confidential~~", or if disclosed in some other form is marked "~~confidential~~", "~~confidential~~".

10.2 Permitted Disclosures. For purposes of this Article 10, information and data described in clause (a) or (b) above shall be referred to as "Confidential Information". "Confidential Information". John Hancock may disclose Confidential Information as required by applicable law, regulation or judicial process, provided that John Hancock shall, if legally permitted, give Abbott prompt written notice thereof. The obligation not to disclose or use Confidential Information shall not apply to any part of such Confidential Information that (i) ~~is~~ (i) is or becomes patented, published or otherwise part of the public domain other than by acts or omissions of John Hancock in contravention of this Agreement; or (ii) ~~is~~ (ii) is disclosed to John Hancock by a third party, provided such Confidential Information was not obtained on a confidential basis by such third party from Abbott, its Affiliates or Licensees; or (iii) prior to disclosure under the Agreement, was already in the possession of John Hancock, provided such Confidential Information was not obtained directly or indirectly from Abbott, its Affiliates or Licensees under an ongoing obligation of confidentiality; or (iv) ~~is~~ (iv) is disclosed in a press release agreed to by both parties under Section 10.3 below.

10.3 Publicity Review. Without the prior written consent of the other party, neither party shall make any statement to the public regarding the execution and/or any other aspect of the subject matter of this Agreement or any work under the Research Program. John Hancock and Abbott shall not disclose any terms or conditions of this Agreement to any third party without the prior consent of the other party, except as set forth above in this Section 10.3 or as required by applicable law, regulation or court order.

The parties have agreed not to issue a press release announcing the execution of this Agreement.

## ARTICLE 11 TERM AND TERMINATION

CONFIDENTIAL  
JH 004444

-21-

11.1 Expiration. Unless terminated earlier by agreement of the parties or pursuant to Sections 11.2 or 11.4 below, this Agreement shall expire upon satisfaction of Abbott's obligations to pay royalties and all other amounts under this Agreement.

11.2 Material Breach. It is the parties' express intent that consideration shall first and foremost be given to remedying any breach of this Agreement through the payment of monetary damages or such other legal or equitable remedies as shall be appropriate under the circumstances and that there shall only be a limited right to terminate this Agreement under the following circumstances as a matter of last resort. In the event that the Neutral [define], in accordance with the procedures set forth in Section 16.7, has rendered a ruling that a party has breached this Agreement, which ruling specified the remedies imposed on such breaching party for such breach (the "Adverse Ruling"), "Adverse Ruling", and the breaching party has failed to comply with the terms of the Adverse Ruling within the time period specified therein for compliance, or if such compliance cannot be fully achieved by such date, or if the breaching party has failed to commence compliance and/or has failed to use diligent efforts to achieve full compliance as soon after the Adverse Ruling as is reasonably possible, then the non-breaching party shall have the following rights and all other rights available to it under law:

- (a) where Abbott is the breaching party that failed to comply with the Adverse Ruling and where the basis for such breach is Abbott's failure to abide by a material obligation under this Agreement, John Hancock may, upon written notice to Abbott, terminate this Agreement; and
- (b) where John Hancock is the breaching party that failed to comply with the Adverse Ruling and where the basis for such breach is John Hancock's failure to abide by a material obligation under this Agreement, Abbott may, upon written notice to John Hancock, terminate this Agreement.

### 11.3 Effect of Expiration or Termination.

(a) Expiration. Expiration or termination of this Agreement shall not relieve the parties of any obligation accruing prior to such expiration or termination. The provisions of Articles 10 through 12, 15 and 16 shall survive the expiration or termination of the Agreement.

~~[(b) Notwithstanding anything herein to the contrary, termination of this Agreement by Abbott for any reason shall not relieve Abbott of its obligations under Articles 2 through 9, except that, to the extent that John Hancock has not made all of the Program Payments required by Article 3, then all Net Sales determinations, milestone payments (pursuant to Article 6), Annual Minimum Spending Targets and the Aggregate Spending Target shall thereafter be reduced by the fraction obtained by dividing (i) the aggregate of the Program Payments actually made by John Hancock by (ii) \$220,000,000.]~~

11.4 Bankruptcy. Either party shall have the right to terminate this Agreement by delivering sixty (60) days prior written notice to the other party in the event of the other party's

CONFIDENTIAL  
JH 004445



-22-

~~bankruptcy (not to include reorganization) or insolvency, provided that applicable federal bankruptcy laws shall apply. [Why?]~~

ARTICLE 12  
WARRANTIES AND INDEMNITY

12.1 John Hancock Representations and Warranties. John Hancock represents and warrants to Abbott that:

- (a) The execution and delivery of this Agreement and the performance of the transactions contemplated hereby have been duly authorized by all appropriate John Hancock corporation action. This Agreement constitutes John Hancock's valid and binding legal obligation, enforceable against it in accordance with its terms.
- (b) The performance by John Hancock of any of the terms and conditions of this Agreement on its part to be performed does not and will not constitute a breach or violation of its organizational documents or any other material agreement or understanding, written or oral, to which it is a party or any law, statute, rule or regulation by which it is bound.
- (c) No consent, approval, license or authorization of, or designation, declaration or filing with, any court or governmental authority is or will be required on the part of John Hancock in connection with the execution, delivery and performance by John Hancock of this Agreement or any other agreements or instruments executed and delivered by John Hancock in connection herewith or therewith, including, without limitation, any filings pursuant to federal or state securities laws or pursuant to any federal or foreign anti-trust laws.
- (d) Neither John Hancock nor any person acting on its behalf (i) has taken or will take any action which would subject this Agreement and the consummation of the transactions contemplated hereby to the registration or qualification requirements of any foreign or domestic (federal or state) securities laws, (ii) has dealt with any broker, finder or other similar person in connection with the transactions contemplated by this Agreement or (iii) is under any obligation to pay any broker's fee, finder's fee or commission in connection with such transactions.

12.2 Abbott Representations and Warranties. Abbott represents and warrants to John Hancock that as of the Effective Date: [to be discussed - delivery of opinion of counsel with respect to certain of the following topics]

CONFIDENTIAL  
JH 004446

-23-

- (a) The execution and delivery of this Agreement and the performance of the transactions contemplated hereby have been duly authorized by all appropriate Abbott ~~corporation~~ Corporation action. This Agreement constitutes Abbott's valid and binding legal obligation, enforceable against it in accordance with its terms.
- (b) The performance by Abbott of any of the terms and conditions of this Agreement on its part to be performed does not and will not constitute a breach or violation of its organizational documents or any other agreement or understanding, written or oral, to which it is a party or any law, statute, rule or regulation by which it is bound.
- (c) [FDA hereunder?] No consent, approval, license or authorization of, or designation, declaration or filing with, any court or governmental authority is or will be required on the part of Abbott in connection with the execution, delivery and performance by Abbott of this Agreement or any other agreements or instruments executed and delivered by Abbott in connection herewith or therewith, including, without limitation, any filings pursuant to federal or state securities laws or pursuant to any federal or foreign anti-trust laws.
- (d) Set forth on Exhibit 12.2(d) is the full name, detailed description of the stage of development, and current status and scope of patent coverage, for each Program Compound. ~~Also set forth on Exhibit 12.2(d), are the projected sales and projected peak sales per calendar year through 2014, detailed for each Program Compound.~~
- ~~description of projected milestones and dates thereof, and projected year of product launch, for each Program Compound. Such projections were prepared in good faith and with due care based on reasonable assumptions, and represent the reasonable estimate of Abbott as to the future performance of the Program Compounds based on information available as of the date of such projections and as of the date hereof; it being agreed that such projections do not constitute any warranty as to the future performance of the Program Compounds and that actual results may vary from projected results.~~
- (e) ~~Set (e)~~ [Patent Department review pending] Set forth on Exhibit 12.2(e) is a list and description of all material domestic and foreign patents, patent rights, patent applications and all patent applications that are in the process of being prepared that are owned by or registered in the name of Abbott, or of which Abbott is a licensor or licensee or in which Abbott has any right, ~~which are related to the Research Program or cover any of the Program Compounds.~~ At the knowledge of Abbott, all of such patents and patent applications have been duly filed in or issued by the United States Patent and Trademark Office or the equivalent foreign patent office, as the case may be, and have been properly maintained and renewed in

CONFIDENTIAL  
JH 004447



-24-

accordance with all applicable laws and regulations. To the knowledge of Abbott, Abbott owns or has a valid license to all Program Inventions, patents, patent applications, copyrights, manufacturing processes, formulae, trade secrets, proprietary rights and know how necessary or desirable with respect to the Program Compounds and the Research Program as heretofore conducted and as proposed to be conducted (collectively, the "Intellectual Property"). Except as set forth in Exhibit 12.2(e), Abbott's use of the Intellectual Property does not require the consent of any other person and the Intellectual Property is owned exclusively by Abbott, free and clear of any liens or encumbrances of any other person. Except as set forth in Exhibit 12.2(e), Abbott has not received any communications alleging that, and no claim is pending or, to the knowledge of Abbott, threatened to the effect that, the operations of Abbott with respect to the Research Program or the Program Compounds infringe upon or conflict with (or will infringe or conflict with) the asserted rights of any other person under any domestic or foreign patent, trademark, service mark, copyright, trade secret, proprietary right or any other intellectual property right, and there is no basis known to Abbott for any such claim (whether or not pending or threatened). No right. Except as set forth in Exhibit 12.2(e), no claim is pending or, to the knowledge of Abbott, threatened to the effect that any of the Intellectual Property is invalid or unenforceable by Abbott, and there is no basis known to Abbott for any such claim (whether or not pending or threatened). To the knowledge of Abbott, all technical information developed by and belonging to Abbott which has not been patented or copyrighted has been kept confidential.

- (f) Except for the Eisai Agreement and customary employment and consulting agreements with Abbott's own employees or consultants, there are no outstanding options, licenses, or agreements of any kind relating to the Intellectual Property or any of the Program Compounds or the transactions contemplated by this Agreement. (f) Except pursuant to the Eisai Agreement, Abbott has not granted or assigned to any other person any right to use, manufacture, have manufactured, produce or sell any of the Program Compounds or Products. the right to sell the Program Compounds.
- (g) To the knowledge of Abbott and with respect to the Research Program and each of the Program Compounds, Abbott is not now, and in performing its obligations hereunder will not be, in any way making an unlawful or wrongful use of any confidential information, know-how, or trade secrets of any other person, including without limitation any former employer or limitation, any present or past employee of Abbott.
- (h) Neither this Agreement, Agreement nor any Exhibit to this Agreement, nor any other agreement, document or written statement made by Abbott and furnished by Abbott to John Hancock or John Hancock's counsel in

CONFIDENTIAL  
JH 004448

-25-

connection with the transactions contemplated hereby, contains any untrue statement of material fact or omits to state any material fact necessary to make the statements contained herein or therein not misleading. There is no fact known to Abbott as of the date of this Agreement that has not been disclosed herein or in any other agreement, document or written statement furnished by Abbott to John Hancock or its counsel in connection with the transactions contemplated hereby which materially adversely affects or could materially and adversely affect the prospects or condition Abbott reasonably believes has had or would have a material adverse effect on the current status (safety, efficacy, ~~commercial or other~~ scientific viability) of the Research Program or any of the Program Compounds.

- (i) Neither Abbott nor any person acting on its behalf (i) has taken or will take any action which would subject this Agreement and the consummation of the transactions contemplated hereby to the registration or qualification requirements of any foreign or domestic (federal or state) securities laws, (ii) has dealt with any broker, finder or other similar person in connection with the transactions contemplated by this Agreement or (iii) is under any obligation to pay any broker's fee, finder's fee or commission in connection with such transactions.
- (j) There is no action, proceeding or investigation pending or, to the knowledge of Abbott, threatened on any basis thereafter known to Abbott which (i) questions the validity of this Agreement or any action taken or to be taken by Abbott pursuant thereto or (ii) which has resulted in, or could reasonably be expected to result in, a material adverse change in the prospects or condition (safety, efficacy, ~~commercial~~ scientific viability or other) of the Research Program or any of the Program Compounds.
- (k) With respect to the Research Program and each of the Program Compounds, Abbott has (and in the future will have) obtained, to the extent permitted by law, from each of its employees and from each of the employees of its Affiliates and Subcontractors an agreement in customary form pursuant to which each such person shall have agreed that all title to the Program Inventions, Program Compounds and Products is and shall be held by Abbott.
- (l) Since \_\_\_\_\_, 2000, no condition, circumstance or fact has arisen nor has Abbott made any change in the conduct of the Research Program that, individually or in the aggregate, materially adversely affects or could materially and adversely affect the prospects or condition (safety, efficacy, ~~commercial or other~~) of the Research Program or any of the Program Compounds.
- (o) No royalty or other payment made hereunder to John Hancock will be subject to any withholding or similar tax imposed by any government or taxing authority.

CONFIDENTIAL  
JH 004449

-26-

12.3 No Conflict. Abbott and John Hancock represent and warrant that this Agreement does not, and will not, conflict with any other right or obligation provided under any other agreement or obligation that Abbott or John Hancock has with or to any third party.

12.4 Compliance with Law. Abbott represents and warrants to John Hancock that it will comply with all applicable laws, regulations and guidelines in connection with its performance of its obligations and rights pursuant to this Agreement, including the regulations of the United States and any other relevant nation concerning any export or other transfer of technology, services or products.

[12.5 Certain Breaches. As mentioned in our memo, in the event of certain breaches, we feel that John Hancock should be entitled to certain remedies - to be discussed.]  
discussed.] EACH PARTY TO THIS AGREEMENT AGREES THAT, EXCEPT FOR THE REPRESENTATIONS AND WARRANTIES CONTAINED IN THIS AGREEMENT, NEITHER PARTY MAKES ANY OTHER REPRESENTATIONS OR WARRANTIES, AND EACH HEREBY DISCLAIMS ANY OTHER REPRESENTATIONS OR WARRANTIES MADE BY ITSELF OR ANY OF ITS OFFICERS, DIRECTORS, EMPLOYEES, AGENTS, FINANCIAL AND LEGAL ADVISORS OR OTHER REPRESENTATIVES, WITH RESPECT TO THE EXECUTION AND DELIVERY OF THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED BY THIS AGREEMENT, NOTWITHSTANDING THE DELIVERY OR DISCLOSURE TO THE OTHER OR THE OTHER'S REPRESENTATIVES OF ANY DOCUMENTATION OR OTHER INFORMATION WITH RESPECT TO ANY ONE OR MORE OF THE FOREGOING.

12.6 Indemnification of John Hancock. Abbott shall indemnify and hold John Hancock and its Affiliates, agents, directors and employees harmless, and hereby forever releases and discharges John Hancock and its Affiliates, agents, directors and employees, from and against all Losses related to or arising out of, directly or indirectly, (a) any negligence, recklessness or intentional misconduct of Abbott or its Affiliates, agents, directors, employees, Subcontractors, licensees (including Licensees) or sublicensees in connection with the Research Program, Program Compounds or Products, or (b) any manufacture, use, storage, distribution or sale of the Program Compounds or Products by anyone, including without limitation all Losses related to any personal injury or death, or (c) any breach by Abbott its representations, warranties or obligations hereunder or under any related agreement, document or instrument and/or enforcement of the terms hereof or (d) the consummation of the transactions contemplated hereby, except, in each case, to the extent any such Losses are the result of any breach by John Hancock of its representations, warranties or obligations hereunder.

12.7 Procedure. If John Hancock or any of its Affiliates, agents, directors or employees (each, an "Indemnitee") intends to claim indemnification under this Article 12, it shall promptly notify Abbott (the "Indemnitor") of any Loss or action in respect of which the Indemnitee intends to claim such indemnification, and the Indemnitor shall have the right to participate in, and, to the extent the Indemnitor so desires, to assume the defense thereof with counsel selected by the Indemnitor; provided, however, that an Indemnitee shall have the right to retain its own counsel, with the fees and expenses of such counsel to be paid by the Indemnitor, if representation of such Indemnitee by the counsel retained by the Indemnitor would be

CONFIDENTIAL  
JH 004450

-27-

inappropriate due to actual or potential differing interests between such Indemnitee and any other party represented by such counsel in such proceedings. The indemnity obligation in this Article 12 shall not apply to amounts paid in settlement of any loss, claim, damage, liability or action if such settlement is effected without the consent of the Indemnitor, which consent shall not be withheld unreasonably or delayed. The failure to deliver notice to the Indemnitor within a reasonable time after the commencement of any such action, if materially prejudicial to its ability to defend such action, shall relieve the Indemnitor of any liability to the Indemnitee under this Article 12 ~~only to the extent such liability arises from the tardiness or absence of such notice, but~~ the omission so to deliver notice to the Indemnitor will not relieve it of any liability that it may have to any Indemnitee otherwise than under this Article 12. The Indemnitee shall cooperate fully with the Indemnitor and its legal representatives in the investigation of any action, claim or liability covered by indemnification under this Article 12, at the expense of the Indemnitor.

12.8 Insurance. Abbott shall at its expense maintain, through self-insurance or otherwise, product liability insurance with respect to the development, manufacture, sale and use of Products and Program Compounds in such amounts and on such terms as Abbott customarily maintains with respect to its other similar products ~~(and in any event on terms no less comprehensive and favorable than those Abbott currently maintains with respect to such other similar products)~~. Abbott shall maintain such insurance for so long as it continues to develop, manufacture or sell any Products or Program Compounds, and thereafter for so long as Abbott customarily currently maintains such insurance.

12.9 Survival. The representations and warranties set forth in this Agreement shall survive the Execution Date.

#### ARTICLE 13 FORCE MAJEURE

Neither party shall be held liable or responsible to the other party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party including but not limited to fire, floods, embargoes, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, general strikes, lockouts or other labor disturbances, acts of God or acts, omission or delays in acting by any governmental authority.

#### ARTICLE 14 ASSIGNMENT

Except as expressly provided hereunder, this Agreement may not be assigned or otherwise transferred, nor may any right or obligations hereunder be assigned or transferred by either party without the consent of the other party; provided, however, that either party shall be obligated to assign this Agreement and its rights and obligations hereunder in connection with the transfer or sale of all or substantially all of its business pertaining to this Agreement, or in the event of its merger or consolidation or change in control or similar transaction and in such event

CONFIDENTIAL  
JH 004451

-28-

such party shall cause its successor or transferee in such transaction to assume all of the obligations of such party. [Why is this necessary? What if 20 assignees?] Any permitted assignee shall assume all obligations of its assignor under this Agreement. Notwithstanding the foregoing, John Hancock shall have right to assign its right to payments without Abbott's consent any of its rights, in whole or in part, hereunder (but not its obligations) to any other person and such other person shall be permitted to enjoy and exercise all of the rights of John Hancock assigned to it.

it; provided that if such assignee is located outside the United States, (i) John Hancock shall notify Abbott at least sixty (60) days in advance and (ii) such payment shall be subject to any applicable U.S. withholding and (iii) such assignee shall not be a company in the health care industry.

#### ARTICLE 15 SEVERABILITY

Each party hereby agrees that it does not intend its execution and delivery hereof or its performance hereunder to violate any public policy, statutory or common laws, rules, regulations, treaty or decision of any government agency or executive body thereof of any country or community or association of countries. If any term or provision of this Agreement is held to be invalid, illegal or unenforceable by a court or other governmental authority of competent jurisdiction, such invalidity, illegality or unenforceability shall not affect any other term or provision of this Agreement, which shall remain in full force and effect. The holding of a term or provision to be invalid, illegal or unenforceable in a jurisdiction shall not have any effect on the application of the term or provision in any other jurisdiction.

#### ARTICLE 16 MISCELLANEOUS

16.1 Notices. Any consent, notice or report required or permitted to be given or made under this Agreement by one of the parties hereto to the other shall be in writing, delivered personally or by facsimile (and promptly confirmed by personal delivery, U.S. first class mail or courier), U.S. first class mail or courier, postage prepared (where applicable), addressed to such other party at its address indicated below, or to such other address as the addressee shall have last furnished in writing to the addressor and (except as otherwise provided in this Agreement) shall be effective upon receipt by the addressee.

If to John Hancock: John Hancock Life Insurance Company  
200 Clarendon Street, T-57  
Boston, MA 02117  
Attention: Bond & Corporate Finance Group  
Fax: 617/572-1628  
Telephone: \_\_\_\_\_  
Fax: 617-572-1628

CONFIDENTIAL  
JH 004452



-29-

copy to: John Hancock Life Insurance Company  
200 Clarendon Street, T-50  
Boston, MA 02117  
Attention: Investment Law Division  
Fax: 617/572-9268 Telephone: \_\_\_\_\_

Fax: 617-572-9268

If to Abbott: Abbott Laboratories  
Dept. 309, Bldg. AP30  
200 Abbott Park Road  
Abbott Park, IL 60064-3537  
Attention: President, Pharmaceutical  
Products Division

Fax: \_\_\_\_\_ Telephone: 847-  
938-6863

Fax: 847-938-5383

copy to: General Counsel  
Abbott Laboratories  
Dept. 364, Bldg. AP6D  
100 Abbott Park Road  
Abbott Park, IL 60064-6020  
Telephone: 847-937-8905  
Fax: 847-938-6277

16.2 Applicable Law. The Agreement shall be governed by and construed in accordance with the internal laws of the State of Illinois. Abbott, to the extent that it may lawfully do so, hereby consents to service of process, and to be sued, in the Commonwealth of Massachusetts and consents to the exclusive jurisdiction of the courts of the Commonwealth of Massachusetts and the United States District Court for the District of Massachusetts, as well as to the jurisdiction of all courts to which an appeal may be taken from such courts, for the purpose of any suit, action or other proceeding arising out of any of its obligations hereunder or thereunder or with respect to the transactions contemplated hereby or thereby, and expressly waives any and all objections it may have as to venue in any such courts. Abbott further agrees that a summons and complaint commencing an action or proceeding in any of such courts shall be properly served and shall confer personal jurisdiction if served personally or by certified mail to it at its address for notices as provided in this Agreement or as otherwise provided under the laws of the Commonwealth of Massachusetts. THE PARTIES EACH IRREVOCABLY WAIVE ALL RIGHT TO A TRIAL BY JURY IN ANY SUIT, ACTION OR OTHER PROCEEDING INSTITUTED BY OR AGAINST IT IN RESPECT OF ITS OBLIGATIONS HEREUNDER OR THEREUNDER OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THEREBY.

16.3 Entire Agreement. This Agreement contains the entire understanding of the parties with respect to the subject matter hereof. All express or implied agreements and understandings, either oral or written, with respect to the subject matter hereof heretofore made

CONFIDENTIAL  
JH 004453

-30-

are expressly merged in and made a part of this Agreement. This Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by both parties hereto.

16.4 Headings. The captions to the several Articles and Sections thereof are not a part of this Agreement, but are merely guides or labels to assist in locating and reading the several Articles and Sections hereof.

16.5 Independent Contractors. It is expressly agreed that John Hancock and Abbott shall be independent contractors and that the relationship between the two parties shall not constitute a partnership, joint venture or agency. Neither John Hancock nor Abbott shall have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on the other, without the prior consent of the other party to do so.

16.6 Performance By Affiliates, Licensees and Subcontractors. The parties recognize that Abbott may carry out certain obligations under this Agreement through performance by its Affiliates, Licensees and Subcontractors (but in no event shall that relieve Abbott of any of its obligations hereunder). Abbott guarantees that the activities of its Affiliates, Licensees and Subcontractors under this Agreement shall comply with this Agreement.

16.7 Alternative Dispute Resolution. The parties shall attempt to amicably resolve disputes arising between them regarding the validity, construction, enforceability or performance of the terms of this Agreement, and any differences or disputes in the interpretation of the rights, obligations, liabilities and/or remedies hereunder, which have been identified in a written notice from one party to the other, by good faith settlement discussions between the President of Abbott's Pharmaceutical Products Division and the Managing Director of John Hancock or his designee. The parties agree that any dispute that arises in connection with this Agreement, which cannot be amicably resolved by such representatives within thirty (30) days after the receipt of such written notice, shall be resolved by binding Alternative Dispute Resolution ("ADR")("ADR") in the manner described in Exhibit 16.7~~[please provide]~~ attached hereto.

16.8 Waiver. The waiver by either party hereto of any right hereunder or the failure to perform or of a breach by the other party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by said other party whether of a similar nature or otherwise.

16.9 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

[the remainder of this page is intentionally blank]

CONFIDENTIAL  
JH 004454



-31-

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first set forth above.

JOHN HANCOCK LIFE  
INSURANCE COMPANY

ABBOTT LABORATORIES ~~INC.~~

By: \_\_\_\_\_

By: \_\_\_\_\_

Name: \_\_\_\_\_ Name: \_\_\_\_\_

Title: \_\_\_\_\_ Title: \_\_\_\_\_

CONFIDENTIAL  
JH 004455

-32-

EXHIBIT 1. \_\_

ANNUAL RESEARCH PLAN - FIRST PROGRAM YEAR

**CONFIDENTIAL**  
**JH 004456**

-33-

EXHIBIT 1<sub>a</sub>

PROGRAM COMPOUNDS

ABT 980 - BPH Back-up (phase III)  
ABT 627 - Prostate and other cancer (phase III)  
ABT 773 - Oral/pediatric/IV (late phase II)  
ABT 594 - Neurological/bone/acute pain (late phase II)  
E7010 - Cancer (phase II)  
ABT 518 - Cancer (phase I)  
FTI - Cancer (late preclinical)  
Urokinase - Cancer (preclinical)

CONFIDENTIAL  
JH 004457

-34-

## EXHIBIT 16.7

## ALTERNATIVE DISPUTE RESOLUTION

The parties recognize that a bona fide dispute as to certain matters may arise from time to time during the term of this Agreement which relates to either party's rights and/or obligations. To have such a dispute resolved by this Alternative Dispute Resolution ("ADR") provision, a party first must send written notice of the dispute to the other party for attempted resolution by good faith negotiations between the Managing Director of John Hancock and the Senior Vice President, Pharmaceutical Products Division, of Abbott (or their equivalents) of the affected subsidiaries, divisions, or business units within thirty (30) days after such notice is received (all references to "days" in this ADR provision is to calendar days).

Any negotiations regarding a dispute shall be treated as settlement negotiations for purposes of the Federal Rules of Evidence and any similar state rules of evidence. Such negotiations shall not be admissible in any subsequent ADR hearing.

If the matter has not been resolved within thirty (30) days of the notice of dispute, or if the parties fail to meet within such thirty (30) days, either party may initiate an ADR proceeding as provided herein. The parties shall have the right to be represented by counsel in such a proceeding.

1. To begin an ADR proceeding, a party shall provide written notice to the other party of the issues to be resolved by ADR. Within fourteen (14) days after its receipt of such notice, the other party may, by written notice to the party initiating the ADR, add additional issues to be resolved within the same ADR.

2. Within twenty-one (21) days following receipt of the original ADR notice, the parties shall select a mutually acceptable neutral to preside in the resolution of any disputes in this ADR proceeding. If the parties are unable to agree on a mutually acceptable neutral within such period, the parties shall request the President of the Center for Public Resources ("CPR"), 366 Madison Avenue, New York, New York 10017 to select a neutral pursuant to the following procedures:

(a) The CPR shall submit to the parties a list of not less than five (5) candidates within fourteen (14) days after receipt of the request from the parties, along with a Curriculum Vitae for each candidate. No candidate shall be an employee, director, or shareholder of either party or any of their subsidiaries or affiliates.

(b) Such list shall include a statement of disclosure by each candidate of any circumstances likely to affect his or her impartiality.

(c) Each party shall number the candidates in order of preference (with the number one (1) signifying the greatest preference) and shall deliver the list to the CPR within seven (7) days following receipt of the list of candidates. If a party believes a conflict of interest exists regarding any of the candidates, that party shall provide a written explanation of the conflict to the CPR along with its list showing its order of preference for the candidates. Any party failing to return a list of preferences on time shall be deemed to have no order of preference.

CONFIDENTIAL  
JH 004458

-35-

(d) If the parties collectively have identified fewer than three (3) candidates deemed to have conflicts, the CPR immediately shall designate as the neutral the candidate for whom the parties collectively have indicated the greatest preference. If a tie should result between two candidates, the CPR may designate either candidate. If the parties collectively have identified three (3) or more candidates deemed to have conflicts, the CPR shall review the explanations regarding conflicts and, in its sole discretion, may either (i) immediately designate as the neutral the candidate for whom the parties collectively have indicated the greatest preference, or (ii) issue a new list of not less than five (5) candidates, in which case the procedures set forth in subparagraphs 2(a) - 2(d) shall be repeated.

3. No earlier than twenty-eight (28) days or later than fifty-six (56) days after selection, the neutral shall hold a hearing to resolve each of the issues identified by the parties. The ADR proceeding shall take place in \_\_\_\_\_, or at such other location agreed upon by the parties. The language of the ADR shall be English.

4. At least seven (7) days prior to the hearing, each party shall submit the following to the other party and the neutral:

(a) a copy of all exhibits on which such party intends to rely in any oral or written presentation to the neutral;

(b) a list of any witnesses such party intends to call at the hearing, and a short summary of the anticipated testimony of each witness;

(c) a proposed ruling on each issue to be resolved, together with a request for a specific damage award or other remedy for each issue. The proposed rulings and remedies shall not contain any recitation of the facts or any legal arguments and shall not exceed one (1) page per issue.

(d) a brief in support of such party's proposed rulings and remedies, provided that the brief shall not exceed twenty (20) pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

Except as expressly set forth in subparagraphs 4(a) - 4(d), no discovery shall be required or permitted by any means, including depositions, interrogatories, requests for admissions, or production of documents.

5. The hearing shall be conducted on two (2) consecutive days and shall be governed by the following rules:

(a) Each party shall be entitled to five (5) hours of hearing time to present its case. The neutral shall determine whether each party has had the five (5) hours to which it is entitled.

(b) Each party shall be entitled, but not required, to make an opening statement, to present regular and rebuttal testimony, documents or other evidence, to cross-examine witnesses, and to make a closing argument. Cross-examination of witnesses shall occur immediately after their

CONFIDENTIAL  
JH 004459

-36-

direct testimony, and cross-examination time shall be charged against the party conducting the cross-examination.

(c) The party initiating the ADR shall begin the hearing and, if it chooses to make an opening statement, shall address not only issues it raised but also any issues raised by the responding party. The responding party, if it chooses to make an opening statement, also shall address all issues raised in the ADR. Thereafter, the presentation of regular and rebuttal testimony and documents, other evidence, and closing arguments shall proceed in the same sequence.

(d) Except when testifying, witnesses shall be excluded from the hearing until closing arguments.

(e) Settlement negotiations shall not be admissible under any circumstances. Affidavits prepared for purposes of the ADR hearing also shall not be admissible. As to all other matters, the neutral shall have sole discretion regarding the admissibility of any evidence.

6. Within seven (7) days following completion of the hearing, each party may submit to the other party and the neutral a post-hearing brief in support of its proposed rulings and remedies, provided that such brief shall not contain or discuss any new evidence and shall not exceed ten (10) pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

7. The neutral shall rule on each disputed issue within fourteen (14) days following completion of the hearing. Such ruling shall adopt in its entirety the proposed ruling and remedy of one of the parties on each disputed issue but may adopt one party's proposed rulings and remedies on some issues and the other party's proposed rulings and remedies on other issues. The neutral shall not issue any written opinion or otherwise explain the basis of the ruling.

8. The neutral shall be paid a reasonable fee plus expenses. These fees and expenses, along with the reasonable legal fees and expenses of the prevailing party (including all expert witness fees and expenses), the fees and expenses of a court reporter, and any expenses for a hearing room, shall be paid as follows:

(a) If the neutral rules in favor of one party on all disputed issues in the ADR, the losing party shall pay 100% of such fees and expenses.

(b) If the neutral rules in favor of one party on some issues and the other party on other issues, the neutral shall issue with the rulings a written determination as to how such fees and expenses shall be allocated between the parties. The neutral shall allocate fees and expenses in a way that bears a reasonable relationship to the outcome of the ADR, with the party prevailing on more issues, or on issues of greater value or gravity, recovering a relatively larger share of its legal fees and expenses.

9. The rulings of the neutral and the allocation of fees and expenses shall be binding, non-reviewable, and non-appealable, and may be entered as a final judgment in any court having jurisdiction.

**CONFIDENTIAL**  
**JH 004460**

-37-

10. Except as provided in paragraph 9 or as required by law, the existence of the dispute, any settlement negotiations, the ADR hearing, any submissions (including exhibits, testimony, proposed rulings, and briefs), and the rulings shall be deemed Confidential Information. The neutral shall have the authority to impose sanctions for unauthorized disclosure of Confidential Information.

**CONFIDENTIAL**  
**JH 004461**



**PLs' LJ**

**Blewitt, Stephen**

**From:** Philip Deemer [phil.deemer@abbott.com]  
**Sent:** Friday, October 27, 2000 10:35 AM  
**To:** Sblewitt@jhancock.com  
**Subject:** ABT-980

Attached is the letter that was issued Wednesday to the clinical community regarding 980.

To: Kimberly C Smith/LAKE/PPRD/ABBOTT@ABBOTT  
cc:  
Subject: letter for US investigators 097,098,-989,-179 trials

October 25, 2000

Dear Investigator:

Re: Clinical Trials with ABT-980 (Fiduxosin), alpha1 antagonist for the treatment of BPH.

In recent weeks, during routine laboratory monitoring of patients included in trials in the USA, Abbott Laboratories has received safety information that indicates the development of serum transaminase abnormalities exceeding three times the upper limit of normal in approximately 1.5 to 3 percent of patients taking ABT-980 for BPH.

Although, to date, these elevations improved and/or values returned to normal upon discontinuation of the drug, it is unlikely that a medication with this profile would offer patients advantages over current treatments. Therefore Abbott has decided to discontinue the clinical development program for ABT-980, effective immediately.

You will be contacted by the CRO or Abbott personnel in the coming days in order to make arrangements to close out the study. You will be asked to contact your patients in the next few days, instructing them to discontinue drug treatment immediately and to present for a discontinuation assessment at your clinic, within seven days. The final visit procedures are itemized in the protocol. However please note the following deviations from the protocol with respect to the final visit: urinary flow assessment and patient questionnaire completion are no longer necessary, and the biliary ultrasound assessment may be completed within 30 days following the last dose of study drug, as opposed to within 48 hours. Should liver enzymes be elevated above 3 fold Upper Limit of Normal values, repeat profiles are to be determined at least weekly, until normalization of the values.

We want to thank you and your staff for your work and commitment to the ABT-980 clinical trial program, and we apologize for any inconvenience the program discontinuation may cause you and your patients.

Sincerely,

Marleen Verlinden, Ph.D.  
Urology Venture Head  
Abbott Laboratories

**CONFIDENTIAL**  
**JH 000778**

**CONFIDENTIAL**

**ABT – 980**

**Descriptive Memorandum**

*May 2000*

**Abbott Laboratories**

**CONFIDENTIAL  
JH 000779**

5/18/00

980 Hancock

*CONFIDENTIAL*

**ABT – 627**

**Descriptive Memorandum**

*May 2000*

**Abbott Laboratories**

**CONFIDENTIAL  
JH 000780**

May 31<sup>st</sup>, 2000

Hancock\_ABT 627

*CONFIDENTIAL*

**ABT – 773**

**Descriptive Memorandum**

*May 2000*

**Abbott Laboratories**

**CONFIDENTIAL  
JH 000781**

June 5, 2000

Hancock – ABT-773

**CONFIDENTIAL**

**ABT – 594**

**Descriptive Memorandum**

*April 2000*

**Abbott Laboratories**

**CONFIDENTIAL**  
**JH 000782**

*CONFIDENTIAL*

# A-254751 Antimitotic Agent

## **Descriptive Memorandum**

*May 2000*

Abbott Laboratories

CONFIDENTIAL  
JH 000783



*CONFIDENTIAL*

# Matrix Metalloproteinase Inhibitors Program

## **Descriptive Memorandum**

*May 2000*

Abbott Laboratories

**CONFIDENTIAL**  
JH 000784

*CONFIDENTIAL*

# Farnesyl Transease Inhibitor

## Descriptive Memorandum

*May 2000*

Abbott Laboratories

**CONFIDENTIAL**  
JH 000785

May 31st, 2000

Hancock\_FTI

*CONFIDENTIAL*

# **Urokinase Inhibitor Program**

## **Descriptive Memorandum**

*May 2000*

**Abbott Laboratories**

**CONFIDENTIAL  
JH 000786**

May 31st, 2000

Hancock\_Urokinase

**PLs' LL**

CHS Draft 11/15/00 11/16/00

RESEARCH FUNDING AGREEMENT

by and between

ABBOTT LABORATORIES

and

JOHN HANCOCK LIFE INSURANCE COMPANY

dated as of

November \_\_\_\_, 2000

Pl/Deft  
Exhibit No.: 15  
Witness: TUCKER  
Date: 6-27-07  
Maria A. Hasakian, CSR No. 8469

CONFIDENTIAL  
JH 005232

-i-

TABLE OF CONTENTS

ARTICLE 1 - DEFINITIONS .....	1
ARTICLE 2 - ANNUAL RESEARCH PROGRAM .....	9
2.1 <u>Program Term</u> .....	9
2.2 <u>Research Plan</u> .....	9
2.3 <u>Conduct of Research</u> .....	9
2.4 <u>Subcontracting Research</u> .....	9
2.5 <u>Research Reports and Records</u> .....	10
ARTICLE 3 - RESEARCH FUNDING .....	10
3.1 <u>John Hancock Program Payments</u> .....	10
3.2 <u>Abbott Program Payments</u> .....	11
3.3 <u>Carryover Provisions</u> .....	11
3.4 <u>Termination of John Hancock's Program Payment Obligation</u> .....	12
3.5 <u>Hancock Funding Obligation</u> .....	12
ARTICLE 4 - PRODUCT RESEARCH AND DEVELOPMENT .....	12
4.1 <u>Commercially Reasonable Efforts</u> .....	12
4.2 <u>Marketing and Sale Responsibility</u> .....	13
4.3 <u>Failure of Program Compound to Progress</u> .....	13
4.4 <u>Arm's-Length</u> .....	13
4.5 <u>In-License Agreements</u> .....	13
ARTICLE 5 - PROGRAM INVENTIONS .....	13
5.1 <u>Ownership</u> .....	13
5.2 <u>Patent Prosecution and Maintenance</u> .....	14
5.3 <u>Enforcement</u> .....	14
ARTICLE 6 - MILESTONE PAYMENTS TO JOHN HANCOCK .....	14
6.1 <u>[Intentionally omitted]</u> .....	14
6.2 <u>Management Fee</u> .....	14
6.3 <u>Milestone Notification and Payments</u> .....	14
ARTICLE 7 - ROYALTIES .....	16
7.1 <u>Royalty Rates</u> .....	16
7.2 <u>Royalty Term</u> .....	16
ARTICLE 8 - ROYALTY REPORTS AND ACCOUNTING .....	16
8.1 <u>Reports, Exchange Rates</u> .....	16
8.2 <u>Audits</u> .....	17
8.3 <u>Confidential Financial Information</u> .....	18
8.4 <u>Accounting Principles</u> .....	18
ARTICLE 9 - PAYMENTS .....	18
9.1 <u>Payment Terms</u> .....	18
9.2 <u>Payment Method</u> .....	18
9.4 .....	
9.3 <u>Late Payments</u> .....	18
ARTICLE 10 - CONFIDENTIALITY .....	19
10.1 <u>Nondisclosure Obligations</u> .....	19
10.2 <u>Permitted Disclosures</u> .....	19
10.3 <u>Publicity Review</u> .....	19
ARTICLE 11- TERM AND TERMINATION .....	20
11.1 <u>Expiration</u> .....	20
11.2 <u>Termination</u> .....	20
11.3 <u>Effect of Expiration of Termination</u> .....	21
ARTICLE 12 - WARRANTIES AND INDEMNITY .....	21

CONFIDENTIAL  
JH 005233

-ii-

12.1	<u>John Hancock Representations and Warranties</u>	21
12.2	<u>Abbott Representations and Warranties</u>	21
12.3	<u>No Conflict</u>	25
12.4	<u>Compliance with Law</u>	25
12.5	<u>No Other Warranties</u>	25
12.6	<u>Indemnification of John Hancock</u>	26
12.7	<u>Procedure</u>	
12.7	<u>Indemnification of John Hancock Relating to In-Licensed Compounds</u>	26
12.8	<u>Procedure</u>	26
12.9	<u>Insurance</u>	27
12.9	<u>Survival</u>	24
12.10	<u>Acknowledgment</u>	27
ARTICLE 13	- FORCE MAJEURE	27
ARTICLE 14	- ASSIGNMENT	27
ARTICLE 15	- SEVERABILITY	28
ARTICLE 16	- MISCELLANEOUS	28
16.1	<u>Notices</u>	28
16.2	<u>Applicable Law</u>	29
16.3	<u>Entire Agreement</u>	30
16.4	<u>Headings</u>	30
16.5	<u>Independent Contractors</u>	30
16.6	<u>Performance By Affiliates</u>	30
16.7	<u>Alternative Dispute Resolution</u>	30
16.8	<u>Waiver</u>	30
16.9	<u>Counterparts</u>	31

EXHIBIT 1.:	Annual Research Plan - First Program Year
EXHIBIT 1.:	Eisai Territory
EXHIBIT 1.:	List of Program Compounds
EXHIBIT 1.:	Example of Program Related Costs
EXHIBIT 6.3	Program Compound Status
EXHIBIT 9.2:	Wiring Instructions for John Hancock
EXHIBIT 12.2(d):	Program Compound Detail
EXHIBIT 12.2(e):	Patents, etc.
EXHIBIT 12.2(f):	Litigation, etc.
EXHIBIT 12.2(i):	Compound Reports
EXHIBIT 16.7:	Alternative Dispute Resolution

[opinion to be delivered]

**CONFIDENTIAL**  
JH 005234



CHS Draft ~~11/14/00~~ 11/16/00

RESEARCH FUNDING AGREEMENT

This Research Funding Agreement is made as of November \_\_, 2000, by and between Abbott Laboratories, an Illinois corporation ("Abbott"), with its principal offices at 100 Abbott Park Road, Abbott Park, Illinois 60064-6049, and John Hancock Life Insurance Company, a Massachusetts corporation ("John Hancock"), with its principal offices at 200 Clarendon Street, Boston, Massachusetts 02117.

WITNESSETH

WHEREAS, Abbott is a global healthcare company actively engaged in the research and development of human pharmaceutical products;

WHEREAS, Abbott is interested in obtaining additional funding to support such research and development activities with respect to certain pharmaceutical products which are under development; and

WHEREAS, John Hancock is interested in providing such additional funding in exchange for the right to receive future milestone and royalty payments from Abbott.

NOW, THEREFORE, in consideration of the foregoing and the mutual covenants and undertakings contained herein, the parties hereto agree as follows:

ARTICLE I  
DEFINITIONS

In addition to the other terms defined elsewhere herein, the following terms shall have the following meanings when used in this Agreement (and any term defined in the singular shall have the same meaning when used in the plural and vice versa, unless stated otherwise):

1.1 "Affiliate" shall mean, with respect to each party, any corporation or other form of business organization, which directly or indirectly owns, controls, is controlled by, or is under common control with, such party. An entity shall be regarded as being in control of another entity if the former entity has the direct or indirect power to order or cause the direction of the policies of the other entity whether (i) through the ownership of fifty percent (50%) or more in the United States, or thirty percent (30%) or more outside the United States, of the outstanding voting securities (or other ownership interest for a business organization other than a corporation) of that entity; or (ii) by contract, statute, regulation or otherwise.

1.2 "Aggregate Carryover Amount" shall have the meaning given in Section 3.3.

1.3 "Aggregate Spending Target" shall mean Six Hundred Million Dollars (\$600,000,000).

**CONFIDENTIAL**  
**JH 005235**

-2-

1.4 "Annual Carryover Amount" shall have the meaning given in Section 3.3.

1.5 "Annual Minimum Spending Target" for each Program Year shall mean the sum of (i) the Program Payment of John Hancock for such Program Year as specified in Section 3.1 ~~((whether or not due and payable, and~~ without giving effect to any deferral or other change under Section 3.1 or 3.3), (ii) Fifty Million Dollars (\$50,000,000), and (iii) any Annual Carryover Amount for the prior Program Year pursuant to Section 3.3.

1.6 "Annual Research Plan" shall mean a reasonably and consistently detailed statement of ~~Abbott's~~ the objectives, activities, timetable and budget for ~~its research and development activities related to the~~ the Research Program Compounds for every Program Year remaining in the Program Term, it being understood that less detail shall be required for Program Years that are not the current Program Year. The first Annual Research Plan is attached as Exhibit 1.16. [should this be provided until all Royalty Terms end? or until the Program Term, as extended, ends?]

1.7 "Bundled Product" shall have the meaning given in paragraph (b) of the definition of Net Sales.

1.8 "Combination Product" shall mean any product containing one or more Program Compounds combined as a single pharmaceutical product with one or more other therapeutically active ingredients.

1.9 "Commercially Reasonable Efforts" shall mean efforts which are consistent with those normally used by other pharmaceutical companies with respect to other pharmaceutical compounds or products which are of comparable potential commercial value and market potential at a similar stage of development or product life, taking into account, without limitation, issues of safety and efficacy, compound or product profile, proprietary status, the regulatory environment and the status of the compound or product and other relevant scientific factors.

1.10 "Compound Reports" shall have the meaning given in Section 12.2.

1.11 "Confidential Information" shall have the meaning given in Section 10.2.

1.12 "Delivery System Product" shall have the meaning given in the definition of Net Sales.

1.13 "Dollars" or "\$" shall mean United States dollars.

1.14 "ED Preclinical Program" shall mean [\_\_\_\_\_]

1.15 "Eisai Agreement" shall mean the License Agreement dated June 29, 2000 between Eisai Co., Ltd. and Abbott related to the Program Compound known as ABT-751.

1.16 "Eisai Territory" shall mean the countries listed on Exhibit 1.16 hereto.

CONFIDENTIAL  
JH 005236

-3-

1.17 "Execution Date" shall mean the date set forth in the introductory paragraph to this Agreement.

1.18 "Extension Period" shall have the meaning given in Section 3.1.

1.19 "FDA" shall mean the U.S. Food and Drug Administration or any successor entity thereto.

~~1.19~~

1.20 "First Commercial Sale" shall mean the first sale of a Product in a given country by Abbott, its Affiliates or Licensees to an unaffiliated third person after Regulatory Approval has been granted in such country.

~~1.20~~

1.21 "FTI Preclinical Program" shall mean [\_\_\_\_\_].

~~1.21~~

1.22 "In-License Agreements" shall mean the Eisai Agreement, the Wakunaga Agreement and the Taisho Agreement.

~~1.22~~

1.23 "International Territory" shall mean all areas of the world outside the U.S. Territory (including Puerto Rico and the U.S. Virgin Islands).

~~1.23~~

1.24 "Investigational New Drug Application" shall mean an investigational new drug application filed with the FDA in order to commence human clinical testing of a drug in the United States.

~~1.24~~

1.25 "Licensee" shall mean any party licensed or otherwise expressly authorized in writing by Abbott, its Affiliates or other Licensees to market, distribute or sell Products and from whom Abbott receives a royalty or similar payment based upon sales of Products by such party, its Affiliates or its licensees (it being understood that a party that is a merely a distributor, wholesaler or similar reseller of Products is not a Licensee hereunder). In no case shall Eisai Co., Ltd. or Taisho Pharmaceutical Co., Ltd. be considered Licensees under the terms of the Eisai Agreement or Taisho Co-Development Agreement with respect to the Eisai Territory ~~or the Taisho Territory, (further including Italy) or Japan, respectively, except pursuant to Section 4.5.~~

~~1.25~~

1.26 "Losses" shall mean any claims, demands, liabilities, costs, damages, judgments, settlements and other reasonable expenses (including attorneys' fees).

~~1.26~~

1.27 "Milestone Payment" shall have the meaning given in Section 6.3.

CONFIDENTIAL  
JH 005237

-4-

~~1.27~~

1.28 "NDA" shall mean a New Drug Application (as defined by the FDA) filed with the FDA for the purpose of obtaining Regulatory Approval of a Product in the U.S. Territory.

~~1.28~~

1.29 "Net Sales" shall mean:

- (a) the total gross sales of the Products (or, for purposes of clauses (b) and (c), the Bundled Products and Combination Products), in each case as set forth on the invoices for such sales by Abbott, its Affiliates and Licensees to unaffiliated third parties in any given period, plus, if applicable, the fair market value of all properties and services received in consideration of a sale of the Products (or, for purposes of clauses (b) and (c), the Bundled Products and Combination Products) by Abbott, its Affiliates and Licensees to unaffiliated third parties during such period, less the following deductions directly paid or actually incurred by Abbott, its Affiliates or Licensees during such period with respect to the sale of the Products (or, for purposes of clauses (b) and (c), the Bundled Products and Combination Products) to the extent included in the gross invoiced sales price therefor:
  - (i) discounts, credits, rebates, allowances, adjustments, rejections, recalls and returns;
  - (ii) price reductions or rebates, retroactive or otherwise, imposed by government authorities;
  - (iii) sales, excise, turnover, inventory, value-added and similar taxes assessed on the royalty-bearing sale of Products;
  - (iv) transportation, importation, insurance and other handling expenses directly chargeable to the royalty-bearing sale of Products;
  - (v) charge backs granted to unaffiliated drug wholesalers; and
  - (vi) the portion of management fees paid to unaffiliated group purchasing organizations that relate specifically to the royalty-bearing sale of Products.
- (b) With respect to a Product which is sold together with any other products and/or services in a country at a unit price, whether packaged together or separately (a "Bundled Product"), the Net Sales of such Bundled Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Bundled Product shall be determined on a country-by-country basis as follows:

CONFIDENTIAL  
JH 005238

-5-

- (i) multiply the Net Sales of such Bundled Product in such country by the fraction  $A/(A+B)$  where A is the average selling price of such Product in such country when sold separately and B is the total of the average selling prices in such country of each such other product(s) and/or service(s) in such Bundled Product when sold separately; or
  - (ii) if (x) either the average selling price of such Product or the total of the average selling prices of each such other products and/or services in such Bundled Product in such country is not available as of such date or (y) such Product is not sold separately in such country, multiply the Net Sales of such Bundled Product in such country by a percentage determined by the mutual agreement of the Parties which represents the proportionate economic value in such country of such Product relative to the economic value in such country contributed by the other products and/or services in such Bundled Product.
- (c) With respect to a Combination Product, the Net Sales of such Combination Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Combination Product shall be determined on a country-by-country basis as follows:
  - (i) multiply the Net Sales of such Combination Product in such country by the fraction  $A/(A+B)$ , where A is the total of the average selling prices of the Program Compounds in such Combination Product, when sold separately in such country and B is the total of the average selling prices of each other therapeutically active ingredient when sold alone as a pharmaceutical product in such country; or
  - (ii) if (x) either the average selling price of all Program Compounds in such Combination Product or the total of the average selling prices of each other therapeutically active ingredient in such Combination Product in such country is not available or (y) such Program Compounds are not sold separately in such country, multiply the Net Sales of such Combination Product by a percentage determined by mutual agreement of the Parties, which represents the proportionate economic value in such country of all Program Compounds in such Combination Product relative to the economic value in such country contributed by all other therapeutically active ingredients in such Combination Product.
- (d) For purposes of this paragraph (d), a "Premium Delivery System" means any delivery system comprising device(s), equipment, instrumentation or other non-ingestible components (but not solely containers or packaging)

**CONFIDENTIAL**  
**JH 005239**

-6-

designed to assist in the administration of a Product[, *such as the Abbott ADD-Vantage® System*]. With respect to a Product which is sold together with a Premium Delivery System (a "Delivery System Product") in a country at a unit price, the Net Sales of such Delivery System Product shall first be calculated in accordance with the definition of Net Sales under paragraph (a), and then the Net Sales of such Product shall be determined on a country-by-country basis as follows:

- (i) if the Product is sold separately without the Premium Delivery System in a country, reduce the Net Sales of such Delivery System Product in such country by the amount that the average selling price of the Delivery System Product in such country exceeds the average selling price of such Product as sold separately in such country; or
- (ii) if the Product is not sold separately without the Premium Delivery System in such country, reduce Net Sales of such Delivery System Product by an amount, determined by mutual agreement of the Parties, which represents the proportionate economic value in such country added by the Premium Delivery System.

~~Notwithstanding anything else herein,~~

- (e) Net Sales shall not include any sales of Products containing the Program Compound (and no other Program Compound) known as (i) ABT-751 by Eisai Co. Ltd., its Affiliates or licensees in the Eisai Territory (further including Italy), or (ii) ABT-773 by Taisho Pharmaceutical Co., Ltd., its Affiliates or licensees in the Taisho Territory Japan. ~~Notwithstanding the foregoing sentence or anything else herein,~~ Net Sales shall include in all instances sales by such parties of such products that are outside such territories, respectively.

~~1.29~~

1.30 "Neutral" shall have the meaning set forth in Section 16.7.

~~1.30~~

1.31 "Parties" shall mean Abbott and John Hancock.

~~1.31~~

1.32 "Phase I Clinical Trial" shall mean those clinical trials which utilize a limited number of human beings to preliminarily address safety and to determine what doses can be safely tolerated.

~~1.32~~

1.33 "Phase II Clinical Trial" shall mean those controlled clinical trials, the primary objective of which is to ascertain additional data regarding the safety and tolerance of one of the Program Compounds and preliminary data regarding such Program Compound's efficacy.

CONFIDENTIAL  
JH 005240



-7-

~~1.33~~

1.34 "Phase III Clinical Trial" shall mean one or a series of controlled pivotal studies of a specific Product by administration of such Product to human beings where the principal purpose of such trial is to provide confirmatory safety and efficacy data necessary to support the filing for Regulatory Approval of a Product.

~~1.34~~

1.35 "Preclinical Programs" shall mean the FTI Preclinical Program, the ED Preclinical Program, the \_\_\_\_\_ and \_\_\_\_\_.

~~1.35~~

1.36 "Premium Delivery System" shall have the meaning given in paragraph (d) of the definition of Net Sales.

~~1.36~~

1.37 "Product" shall mean any product containing one or more of the Program Compounds as an active ingredient, alone or in combination with other active ingredients (including any Bundled Product and any Combination Product).

~~1.37~~

1.38 "Program Compounds" shall mean (i) the compounds listed on ~~Exhibit 1.37~~ 1.38; (ii) the first compound ~~((the selection of~~ which shall also be the best compound consistent with Abbott using its Commercially Reasonable Efforts) from each of the Preclinical Programs to enter Phase I Clinical Trial; (iii) any compounds or products substituted or added by Section 4.3; (iv) all line extensions ~~and new~~ formulations and pharmaceutically acceptable derivatives of the foregoing; and (v) all analogs, isomers, improvements, other derivatives and modifications of the foregoing unless such analog, isomer, improvement, other derivative or modification would be considered a new chemical entity and required by the FDA to reenter Phase I Clinical Trial. Furthermore, a compound or product shall be considered a Program Compound regardless of the indication for which it is used.

~~1.38~~

1.39 "Program Inventions" shall have the meaning given in Section 5.1.

~~1.39~~

1.40 "Program Payments" shall have the meaning given in Section 3.1.

~~1.40~~

1.41 "Program Related Costs" shall mean (i) all direct and indirect costs and expenses that are incurred by Abbott on the Research Program during a given Program Year, and allocated in a manner consistent with Abbott's internal, pharmaceutical products division-wide allocation procedures; and (ii) the milestone and license fees paid during a given Program Year by Abbott to Eisai Co. Ltd. (not to exceed Eighteen Million Dollars (\$18,000,000) in the aggregate with respect to the Program Compound known as ABT-751 pursuant to the Eisai Agreement and to Wakunaga Pharmaceutical Co., Ltd. (not to exceed Twenty Seven Million Five Hundred Thousand Dollars (\$27,500,000) in the aggregate with respect to the Program Compound known as ABT-492 pursuant to the Wakunaga Agreement. In no event shall any payments made by

CONFIDENTIAL  
JH 005241



-8-

Abbott to John Hancock pursuant hereto constitute Program Related Costs. Set forth on ~~Exhibit 1.40~~ Exhibit 1.41 is an example of Program Related Costs for a particular Program Compound.

~~1.41~~

1.42 "Program Term" shall mean a period of ~~four (4)~~ five (5) consecutive Program Years [as extended by the Extension Period].

~~1.42~~

1.43 "Program Year" shall mean a period of twelve (12) consecutive calendar months commencing on December 1 of each year, except that the first Program Year shall commence on the Execution Date and end on November 30, 2001.

~~1.43~~

1.44 "Quarterly Reporting Period" shall mean the calendar quarter with respect to the U.S. Territory together with the fiscal quarter ending on the final day of February, May, August and November (as the case may be) with respect to the International Territory. For example, the Quarterly Reporting Period that comprises the second calendar quarter with respect to the U.S. Territory also includes the period from March 1 through May 31 with respect to the International Territory. If Abbott adopts the calendar year as its fiscal year for the International Territory, then the Quarterly Reporting Period for the International Territory shall also be the calendar quarter.

~~1.44~~

1.45 "Research Program" shall mean all of Abbott's, its Affiliates and Subcontractors' activities directed towards obtaining Regulatory Approval for the Products, including research, development, safety and efficacy studies, clinical trials, process development, formulation work, regulatory, quality, data collection and analysis and project management.

~~1.45~~

1.46 "Regulatory Approval" shall mean: (i) with respect to the U.S. Territory, the receipt of approval from the FDA to market a Product in the U.S. Territory; and (ii) with respect to any country in the International Territory, receipt of the governmental approvals required to market a Product in such country, including any pricing and reimbursement authorization required in such country.

~~1.46~~

1.47 "Royalty Term" shall mean, with respect to each Product in each country, a period of ten (10) years from the date of First Commercial Sale of such Product in such country.

~~1.47~~

1.48 "Subcontractor" shall have the meaning given in Section 2.4.

~~1.48~~

1.49 "Taisho Agreement" shall mean the Co-Development Agreement dated September 30, 1997 between Taisho Pharmaceutical Co., Ltd. and Abbott related to the Program Compound known as ABT-773.

1.50 ~~1.49 "Taisho Territory" shall mean Japan.~~

CONFIDENTIAL  
JH 005242

-9-

1.51 "Territory" shall mean both the U.S. Territory and the International Territory, excluding the Eisai Territory with respect to the Program Compound known as ABT-751. ~~and the Taishe Territory with respect to the Program Compound known as ABT-773~~

1.52 "U.S. Territory" shall mean the United States of America, excluding Puerto Rico and the U.S. Virgin Islands.

1.53 "Wakunaga Agreement" shall mean the License Agreement dated December 1, 1999 between Wakunaga Pharmaceutical Co., Ltd. and Abbott related to the Program Compound known as ABT-492.

## ARTICLE 2 ANNUAL RESEARCH PROGRAM

2.1 Research Program Term. The Research Program shall be conducted by Abbott during the Program Term, and beyond the Program Term until Abbott either abandons development in accordance with the terms hereof or receives Regulatory Approval for each Program Compound.

2.2 Research Plan. The Research Program shall be conducted by Abbott in each Program Year in accordance with the Annual Research Plan for such Program Year. The Annual Research Plan will be provided to John Hancock until Abbott either abandons development in accordance with the terms hereof, or receives Regulatory Approval for, each Program Compound in the U.S. Territory. The Annual Research Plan shall be prepared by Abbott and presented to John Hancock at least thirty (30) days prior to the start of each Program Year. The Annual Research Plan for the first Program Year is attached as Exhibit 1.16. Abbott may modify the Annual Research Plan from time to time in order to best meet the objectives of the Research Program. Any such modifications to the Annual Research Plan shall be promptly provided to John Hancock.

2.3 Conduct of Research. Abbott shall use Commercially Reasonable Efforts to conduct the Research Program in good scientific manner and using good laboratory practices, to achieve the objectives of the Research Program efficiently and expeditiously and to comply with all applicable laws and regulations. Notwithstanding anything in this Agreement to the contrary, Abbott does not represent, warrant or guarantee that the Research Program will be successful in whole or in part or result in the registration or commercialization of any pharmaceutical products or that any Products obtaining Regulatory Approval will be a commercial success.

2.4 Subcontracting Research. Abbott may subcontract or outsource to Affiliates or third persons (each, a "Subcontractor") any portion of the Annual Research Plan. Consistent with Abbott's past practices, each Subcontractor shall enter into a confidentiality agreement with Abbott and agreements pursuant to which such Subcontractor is required to comply with all applicable laws and regulations, including conducting the Research Program in good scientific manner and using good laboratory practices, with respect to its work on the Research Program. Abbott shall supervise and be responsible under this Agreement for the work of each such

CONFIDENTIAL  
JH 005243

-10-

Subcontractor on the Research Program and no subcontracting or outsourcing shall relieve Abbott of any of its obligations hereunder.

2.5 Research Reports and Records. Abbott shall, no later than thirty (30) days before the last day of each Program Year, provide John Hancock with a reasonably detailed report setting forth the status of the Research Program and all Program Related Costs expended by Abbott during such Program Year. The Program Related Costs set forth in such report may include good faith estimates with respect to the last three (3) months of the Program Year, provided that the report under this Section 2.5 for the following Program Year contains the actual Program Related Costs for that three (3) month period. Such report shall also contain such other information related thereto as John Hancock may reasonably request from time to time. Abbott shall, and shall cause each Subcontractor to, maintain complete and accurate records, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes and for purposes of demonstrating compliance with the terms hereof, that fully and properly reflect all work done, results achieved and Program Related Costs expended in performance of the Research Program. The books and records of Abbott and each Subcontractor related to the Research Program, including, without limitation, those related to the expenditure of Program Related Costs, shall be subject to copying, inspection and audit by (and at the expense of) John Hancock at any time and from time to time. Such audit shall occur upon reasonable notice and during normal business hours by an independent auditor selected by John Hancock and reasonably acceptable to Abbott. John Hancock and its independent auditor shall maintain such records and information of Abbott in confidence in accordance with Article 10 and shall not use such records or information except to the extent permitted by this Agreement, including any enforcement of the provisions hereof. In the event that such audit reveals any material breach of Abbott's responsibilities hereunder, Abbott shall (i) pay the reasonable fees and expenses charged by such auditor, and (ii) fully and promptly cure such breach.

### ARTICLE 3 RESEARCH FUNDING

3.1 John Hancock Program Payments. John Hancock shall make the following installment payments on the applicable payment date (the "Payment Date"), for the applicable Program Year, to Abbott to help support the Research Program (the "Program Payments"):

<u>Payment Date</u>	<u>Payment Amount</u>	<u>Program Year</u>
Execution Date	<del>\$50,000,000</del> <u>\$12,500,000</u>	first
December 1, 2001	<del>\$55,000,000</del> <u>\$41,000,000</u>	second
December 1, 2002	<del>\$55,000,000</del> <u>\$44,000,000</u>	third
December 1, 2003	<del>\$60,000,000</del> <u>fourth \$[25,000,000]</u>	<u>fourth</u> (the
<u>"Fourth Payment")</u>		
Such funds		
<u>December 1, 2003</u>	<u>\$[25,000,000]</u>	<u>fourth</u> (the " <u>Fifth Payment</u> ")
<u>December 1, 2004</u>	<u>\$57,500,000</u>	<u>fifth</u> (the " <u>Sixth Payment</u> ")

CONFIDENTIAL  
JH 005244

-11-

All Program Payments shall be expended by Abbott on Program Related Costs and for no other purpose. If John Hancock has not received at least thirty (30) days prior to the Payment Date both (i) the Annual Research Plan for such year and (ii) the report described in Section 2.5 for the previous Program Year, at least thirty (30) days prior to the Payment Date, then John Hancock's obligation to make the Program Payment due on such Payment Date shall be suspended until thirty (30) days have elapsed from the date of John Hancock's receipt of both such Annual Research Plan and report.

In addition to the foregoing requirements and Payment Dates, under no circumstance will the Fourth, Fifth and Sixth Payments be due and payable until thirty (30) days after

- (a) Abbott files the first one NDA, with respect to the Fourth Payment; and
- (b) Abbott receives Regulatory Approval of the first Product in the U.S. Territory, with respect to the Fifth Payment and the Sixth Payment.

[any outside deadline?]

The number of days elapsed from (i) December 1, 2005 until (ii) the date on which Abbott receives such Regulatory Approval, shall be hereinafter referred to as the "Extension Period".

3.2 Abbott Program Payments. Abbott shall spend on Program Related Costs: (i) during each Program Year, at least the Annual Minimum Spending Target for such Program Year and (ii) at least the Aggregate Minimum Spending Target during the Program Term. John Hancock's sole and exclusive remedies for Abbott's failure to fund the Research Program in accordance with this Section 3.2 (but not for any other breach of Abbott's other obligations hereunder) are set forth in Sections 3.3, 3.4 and 7.2.

3.3 Carryover Provisions. Abbott shall be permitted to change its funding obligations under Section 3.2 only as follows:

- (i) If in any Program Year Abbott spends on Program Related Costs, the full amount of the Program Payment provided by John Hancock for such Program Year, but does not spend the full amount of the Annual Minimum Spending Target for such Program Year (including any Annual Carryover Amounts from any prior Program Years), Abbott will spend on Program Related Costs the difference between its expenditure on Program Related Costs for such Program Year and the Annual Minimum Spending Target for such Program Year (the "Annual Carryover Amount") in the subsequent Program Year. John Hancock's obligation to make any Program Payment for such subsequent Program Year, if any, pursuant to Section 3.1, shall be deferred until the time that Abbott has spent and notifies John Hancock that it has spent the Annual Carryover Amount in such subsequent Program Year; and
- (ii) [subject to change] If Abbott does not expend on Program Related Costs the full amount of the Aggregate Spending Target during the Program

-12-

Term, Abbott will expend the difference between its expenditures for Program Related Costs during the Program Term and the Aggregate Spending Target (the "Aggregate Carryover Amount") on Program Related Costs during the subsequent year commencing immediately after the end of the Program Term. If Abbott does not spend the Aggregate Carryover Amount on Program Related Costs during such subsequent year, Abbott will ~~refund~~ pay to John Hancock one-third of the Aggregate Carryover Amount that remains unspent by Abbott, within thirty (30) days of the end of such subsequent year.

3.4 Termination of John Hancock's Program Payment Obligation, [subject to change] If Abbott: (i) abandons development of all Program Compounds during the Program Term; (ii) does not expend on Program Related Costs during any Program Year the full amount of the Program Payment made by John Hancock for such Program Year; (iii) does not reasonably demonstrate in its Annual Research Plan, its intent and reasonable expectation to expend on Program Related Costs during the next Program Year an amount in excess of the Program Payment to be provided by John Hancock for such year; or (iv) does not reasonably demonstrate, in its Annual Research Plan, its intent and reasonable expectation to expend on Program Related Costs during the ~~Research~~ Program Term an amount in excess of the Aggregate Spending Target, John Hancock's obligation to make any remaining Program Payments pursuant to Section 3.1 shall ~~ease; terminate.~~ [subject to change] In addition, in the case of either (i) or (ii) above, Abbott shall refund (not later than the 10th day following such event) to John Hancock the amount, if any, by which the Program Payment made by John Hancock for such year, if any, exceeds one-half of the Program Related Costs actually spent by Abbott during that Program Year.

3.5 Hancock Funding Obligation. John Hancock's entire obligation hereunder shall be limited to providing the Program Payments set forth in Section 3.1. Abbott shall be solely responsible for funding all Program Related Costs in excess of the Program Payments from John Hancock.

#### ARTICLE 4

#### PRODUCT RESEARCH AND DEVELOPMENT

4.1 Commercially Reasonable Efforts. Abbott shall be solely responsible for the clinical development, government approval, manufacturing, marketing, sales and distribution of Products. Abbott will use, and will cause each of its Affiliates and Licensees to use, Commercially Reasonable Efforts to pursue the clinical development, government approval, manufacturing, marketing, sales and distribution of Products throughout the Territory. The obligations of Abbott, its Affiliates and ~~Licenses~~ Licensees with respect to any Product under this Article 4 are expressly conditioned upon the safety, efficacy and commercial feasibility of each Product, consistent with using its Commercially Reasonable Efforts, but no license, assignment or other transfer of rights by Abbott will modify or reduce Abbott's obligations hereunder (except as set forth in Article 14). It is the parties' expectation that under normal circumstances Abbott will file for Regulatory Approval with respect to each Product in Europe within two (2) years from the date of the NDA filing for such Product in the U.S. Territory and in Japan within five



-13-

(5) years from such NDA filing date; provided, however, that these time frames may be extended or otherwise altered based upon unforeseen circumstances that legitimately impact such regulatory filings in such foreign jurisdictions.

4.2 Marketing and Sale Responsibility. Without limiting the generality of Section 4.1, within six (6) months of obtaining Regulatory Approval for a Product in a given country, Abbott, its Affiliates or Licensees shall commence to market and sell such Product in such country. Abbott's obligation to market and sell a Product shall not apply to a Product in any country if Abbott has not commenced or has ceased marketing and selling such Product in such country substantially/primarily on account of adverse business or financial conditions caused by the regulatory authorities or other governmental authorities of such country (including not commencing marketing and selling in a country where the regulatory authorities have price or reimbursement approval and the price or reimbursement approval or that proposed by the regulatory authorities or government authorities is unacceptable to Abbott) which causes the marketing and sale of such Product in such country to be contrary to the financial best interests of John Hancock and Abbott; provided, however, that Abbott, its Affiliates or Licensees shall commence or resume marketing and sale of such Product in such country as soon as reasonably practical after such adverse business or financial conditions cease to exist.

4.3 Failure of Program Compound to Progress. *[remains subject to off-line discussion]*

4.4 Arm's-Length. Abbott shall not research, develop, manufacture, market, sell, distribute, out-license or otherwise treat any Program Compounds or Products differently, as compared to any other Abbott compounds or products, on account of any of John Hancock's rights hereunder. Furthermore, all distribution agreements, licenses, out-licenses and other agreements relating to the research, development, manufacturing, marketing, sale, distribution, licensing, out-licensing or divestiture of and all other transactions involving any Program Compounds or Products to or with any third party (except to Abbott's Affiliates) shall be on arm's-length terms and conditions.

4.5 In-License Agreements. Abbott shall comply in all material respects with the terms and conditions of the In-License Agreements. Abbott shall not amend the In-License Agreements or waive any of its rights thereunder without John Hancock's prior written consent, unless such amendment or waiver does not have and would not have a material adverse effect on John Hancock's interests hereunder. To the extent that Abbott or any of its Affiliates obtains the right to market, distribute or sell Products containing the Program Compound known as (i) ABT-751 in the Eisai Territory or (ii) ~~ABT-773 in the Taisho Territory, then in each case sales, then~~ sales by Abbott, its Affiliates and Licensees of such Products in such ~~territories~~ territory shall be included in all respects hereunder (including without limitation in Net Sales and the Territory).

## ARTICLE 5 PROGRAM INVENTIONS

5.1 Ownership. As between Abbott and John Hancock, all inventions, innovations, ideas, discoveries, technology, know-how, methods, data, applications and products (in each case

**CONFIDENTIAL**  
**JH 005247**

-14-

whether or not patentable) arising from the Research Program or otherwise related to the Program Compounds (collectively, the "Program Inventions") shall be exclusively owned by or assigned to Abbott. Abbott shall not divest, out-license or otherwise transfer any of its right, title or interest in or to any Program Inventions which would prevent or impair Abbott's ability to fulfill its obligations to John Hancock under this Agreement.

5.2 Patent Prosecution and Maintenance. To the extent it owns a Program Invention or has the contractual right to pursue patent protection for a Program Invention, Abbott will use Commercially Reasonable Efforts to obtain patent protection for the Program Inventions in the Territory. As between Abbott and John Hancock, Abbott shall be responsible for all costs and expenses and control all decisions related to pursuing such patent protection, including the preparation, filing (foreign and/or domestic), prosecution, issuance and maintenance of patent applications or patents covering Program Inventions.

5.3 Enforcement. As between Abbott and John Hancock, Abbott shall have the sole right and authority to enforce the patents or any other rights arising from the Program Inventions (including without limitation the Patents) against any infringers. If Abbott initiates any action or lawsuit to enforce such patents or other rights, it shall be solely responsible for the cost and expense thereof. Abbott will promptly notify John Hancock at such time as it becomes aware of any infringement activities and of any such enforcement actions or lawsuit, and Abbott will provide information concerning them as reasonably requested by John Hancock. All moneys recovered upon the final judgment or settlement of any such action or lawsuit, less the out-of-pocket cost and expense thereof, shall be allocated between Abbott and John Hancock proportional to Abbott's lost profits and John Hancock's lost royalties as a result of such infringement.

## ARTICLE 6 MILESTONE PAYMENTS TO JOHN HANCOCK

6.1 [Intentionally omitted].

6.2 Management Fee. On December 1, 2001, 2002, ~~and 2003 and 2004~~, Abbott shall pay to John Hancock a management fee, each of which shall be in the amount of ~~Two~~ One Million Dollars ~~(\$2,000,000)~~ (\$1,000,000).

6.3 Milestone Notification and Payments. Abbott shall promptly notify John Hancock of the occurrence any of the following events that give rise to Abbott's obligation to make a payment pursuant to this Section 6.3 (each, a "Milestone Payment"). Except as hereinafter limited, Abbott shall pay the Milestone Payments to John Hancock in the amounts and at the times set forth below with respect to each Program Compound:

- (a) One Million Dollars (\$1,000,000) shall be paid within thirty (30) days after the allowance by the FDA of each Investigational New Drug Application for such Program Compound;

**CONFIDENTIAL**  
**JH 005248**



-15-

- (b) Two Million Dollars (\$2,000,000) shall be paid within thirty (30) days after the initiation of each Phase I Clinical Trial with such Program Compound;
- (c) Three Million Dollars (\$3,000,000) shall be paid within thirty (30) days after the initiation of each Phase II Clinical Trial with such Program Compound;
- (d) Four Million Dollars (\$4,000,000) shall be paid within thirty (30) days after the initiation of each Phase III Clinical Trial with such Program Compound; and
- (e) Five Million Dollars (\$5,000,000) shall be paid within thirty (30) days after the filing of each NDA with the FDA for such Program Compound; and

~~(f) Ten~~

In addition, except as hereinafter limited, Abbott shall pay the Milestone Payments to John Hancock in the amounts and at the times set forth below:

- (f) (i) Twenty Million Dollars (\$10,000,000)(\$20,000,000) shall be paid within thirty (30) days after the first Regulatory Approval of such Program Compound a Product in the U.S. Territory;
- (ii) Fifteen Million Dollars (\$15,000,000) shall be paid within thirty (30) days after the second Regulatory Approval of a Product in the U.S. Territory; and
- (iii) Fifteen Million Dollars (\$15,000,000) shall be paid within thirty (30) days after the third Regulatory Approval of a Product in the U.S. Territory.

The aggregate of Milestone Payments under Section 6.3(a), (b), (c), (d), and (e) for all Program Compounds shall be limited to Twelve Million Dollars ~~(\$12,000,000)~~ (\$10,000,000), and once such aggregate limit has been paid, no further payments shall be due and payable under Sections 6.3(a), (b), (c), (d) or (e). The aggregate of Milestone Payments under Section 6.3(f) for all Program Compounds shall be limited to Forty Million Dollars ~~(\$40,000,000)~~ (\$50,000,000), and such Milestone Payment shall not be paid more than once per Program Compound. Once such aggregate limit has been paid, no further payments shall be due and payable under Section 6.3(f).

The aggregate of Milestone Payments under Sections 6.3(a), (b), (c), (d) and (e) for all Program Compounds shall be limited to ~~Three Million~~ Zero Dollars ~~(\$3,000,000)~~ (\$0) during the first Program Year and shall be limited to ~~Six, Three Million Dollars (\$6,000,000)~~ (\$3,000,000) during the second Program Year, and Seven Million Dollars (\$7,000,000) during the third Program Year, and once such annual limit has been reached for these particular Program Years, no further payments shall be due under Sections 6.3(a), (b), (c), (d) and (e) for the remainder of such Program Year; provided that any amounts that would have been due to John Hancock but for such annual limits shall be paid in subsequent Program Years so long as the Program

-16-

Compound to which it relates has not been abandoned, divested or out-licensed by Abbott. Subject to the limitations above, the Milestone Payments may be made more than once with respect to each Program Compound. No Milestone Payment shall be made with respect to a milestone achieved prior to the Execution Date. Exhibit 6.3 sets forth the current stage of clinical development for each Program Compound.

[endothelin/ketolide development milestone]

ARTICLE 7  
ROYALTIES

7.1 Royalty Rates. Subject to the limitation set forth below, Abbott shall pay to John Hancock royalties equal to the following percentages of Net Sales, aggregated on a yearly basis, of all Products in the Territory:

<u>Royalty percentage</u>	<u>Yearly Net Sales (in millions) of all Products in the Territory</u>
<del>8%</del>	
<u>8.5%</u> of those Net Sales	up to \$400
and then 4% of those Net Sales	in excess of \$400 up to \$1,000
and then 1% of those Net Sales	in excess of \$1,000 up to \$2,000
and then <del>.5%</del> <u>0.5%</u> of those Net Sales	in excess of \$2,000

Net Sales shall be aggregated yearly (i) in the case of the U.S. Territory, on a calendar year basis, together with (ii) in the case of the International Territory, on a December 1 to November 30 basis, in each case consistent with the determination of Quarterly Reporting Periods.

7.2 Royalty Term. The duration of the obligation to make royalty payments on each Product shall be determined on a country-by-country basis, shall commence for such Product upon the First Commercial Sale thereof in such country, and shall last for the duration of the Royalty Term in each given country for such Product. Notwithstanding anything to the contrary herein, the obligation to make royalty payments on the Products shall not begin until the two-year anniversary of the Execution Date (and only with respect ~~only~~ to Net Sales occurring on or after such date) and shall cease at on December 31, 2014; ~~provided that if Abbott becomes obligated to spend an Aggregate Carryover Amount pursuant to Section 3.3(ii), the obligation to make royalty payments~~ 2015, which shall be extended until December 31, 2015 by the Extension Period, if any.

ARTICLE 8  
ROYALTY REPORTS AND ACCOUNTING

8.1 Reports. Exchange Rates. With respect to every Quarterly Reporting Period for which Abbott is obligated to pay any royalty hereunder, Abbott shall furnish to John Hancock a single written report for such Quarterly Reporting Period within sixty (60) days of the end of

CONFIDENTIAL  
JH 005250

-17-

such Quarterly Reporting Period (that is, within sixty (60) days of each March 31, June 30, September 30 and December 31, as the case may be) showing in reasonably specific detail:

- (a) the total gross sales in each country for each Product sold by Abbott, its Affiliates and Licensees in the Territory and the detailed calculation of Net Sales from gross sales in each country for each Product;
- (b) the royalties payable in Dollars, if any, which shall have accrued hereunder;
- (c) the dates of the First Commercial Sale of ~~the~~ each Product in any country in the Territory during such Quarterly Reporting Period; and
- (d) the exchange rates used in determining the amount of Dollars.

With respect to sales of Products invoiced in Dollars, the gross sales, Net Sales (including all adjustments and deductions permitted to be made hereunder in calculating the same), and royalties payable shall be expressed in Dollars. With respect to sales of Products invoiced in a currency other than Dollars, the gross sales, Net Sales (including all adjustments and deductions permitted to be made hereunder in calculating the same) and royalties payable shall be expressed in their Dollar equivalent, calculated using the Inter Bank rate set forth in the International Report published by International Reports Inc. as Foreign Exchange Rates quoted in New York on the day nearest the last business day of the Quarterly Reporting Period.

## 8.2 Audits.

- (a) Upon the written request of John Hancock and, in the absence of any breach by Abbott hereunder, not more than once in each calendar year, Abbott shall permit John Hancock and an independent certified public accounting firm of nationally recognized standing, selected by John Hancock and reasonably acceptable to Abbott, at John Hancock's expense, to have access during normal business hours to such of the records of Abbott, its Affiliates and Licensees to verify the accuracy of the royalty reports and the amounts and calculation of any payments required hereunder for any year ending not more than five (5) years prior to the date of such request.
- (b) If such accounting firm concludes that additional royalties or other payments were owed during such period, Abbott shall have the option to invoke the proceedings of Section 16.7 below or pay the additional royalties or other payments within thirty (30) days of the date John Hancock delivers to Abbott such accounting firm's written report so concluding. The reasonable fees and expenses charged by such accounting firm shall be paid by John Hancock; provided, however, if the audit discloses that the amounts payable by Abbott for any Quarterly Reporting Period are more than one hundred five percent (105%) of the royalties

**CONFIDENTIAL**  
**JH 005251**

-18-

actually paid for such period, then Abbott shall pay the reasonable fees and expenses charged by such accounting firm.

- (c) Abbott shall cause its Affiliates to, and shall include in each license granted by it pursuant to this Agreement relating to a Program Compound or Product a provision requiring the Licensee ~~(including any Affiliates of Abbott) to to~~ make reports to Abbott, to keep and maintain records of Net Sales made pursuant to such license and to grant access to such records by John Hancock and its accounting firm or other auditor to the same extent required of Abbott under this Agreement.
- (d) All reports and payments not disputed as to correctness by John Hancock within five (5) years after receipt thereof shall thereafter conclusively be deemed correct for all purposes, and Abbott, its Affiliates and Licensees shall be released from any liability or accountability with respect to such reports and payments.

8.3 Confidential Financial Information. John Hancock shall treat all information subject to review under this Article 8, and shall cause its accounting firm to agree to treat all such information, in accordance with the provisions of Article 10.

8.4 Accounting Principles. All accounting hereunder, including without limitation all determinations of gross sales, Net Sales (including all adjustments and deductions permitted to be made hereunder in calculating the same), Program Related Costs and all calculations underlying such determinations, shall be made in accordance with generally accepted accounting principles as in effect in the United States, consistently applied.

## ARTICLE 9 PAYMENTS

9.1 Payment Terms. With respect to every Quarterly Reporting Period for which Abbott is obligated to pay a royalty hereunder, such royalties shall be due and payable in a single payment within sixty (60) days of the end of such Quarterly Reporting Period (that is, within sixty (60) days of each March 31, June 30, September 30 and December 31, as the case may be). Payment of royalties may be made in advance of such due date.

9.2 Payment Method. All royalties and other payments by Abbott to John Hancock under this Agreement shall be made by bank wire transfer in immediately available funds in accordance with the instructions set forth on Exhibit 9.2 attached hereto or in accordance with such other instructions as John Hancock may give from time to time.

9.3 Late Payments. Each party shall pay interest to the other on the aggregate amount of any payments by it that are not paid on or before the date such payments are due under this Agreement, including, without limitation, any disputed payments or payments resulting from any audit, at a rate per annum equal to the lesser of (a) the prime rate of interest plus two-hundred (200) basis points as reported by Citibank, N.A. bank in New York, from time to time (with any

**CONFIDENTIAL**  
**JH 005252**

-19-

change in such reported rate being effective immediately for purposes hereof), or (b) the highest rate permitted by applicable law, calculated on the number of days such payments is delinquent until paid in full in cash. All such amounts shall be payable upon demand.

## ARTICLE 10 CONFIDENTIALITY

10.1 Nondisclosure Obligations. Except as otherwise provided in this Article 10, during the term of the Agreement and for a period of ten (10) years thereafter, (a) John Hancock shall maintain in confidence in accordance with such procedures as are adopted by John Hancock to protect its own confidential information and shall use only for purposes of this Agreement (including, without limitation, enforcement of the terms hereof), information and data related to the Program Compounds or Products; and (b) John Hancock shall also maintain in confidence in accordance with such policies, and use only for purposes of this Agreement, all information and data supplied by Abbott under this Agreement, which if disclosed in writing is marked "confidential", if disclosed orally is promptly thereafter summarized and confirmed in writing to the other party and marked "confidential", or if disclosed in some other form is marked "confidential."

10.2 Permitted Disclosures. For purposes of this Article 10, information and data described in clause (a) or (b) above shall be referred to as "Confidential Information". John Hancock may disclose Confidential Information as required by applicable law, regulation or judicial process, provided that John Hancock shall, if legally permitted, give Abbott prompt written notice thereof. The obligation not to disclose or use Confidential Information shall not apply to any part of such Confidential Information that (i) is or becomes patented, published or otherwise part of the public domain other than by acts or omissions of John Hancock in contravention of this Agreement; or (ii) is disclosed to John Hancock by a third party, provided such Confidential Information was not obtained on a confidential basis by such third party from Abbott, its Affiliates or Licensees; or (iii) prior to disclosure under the Agreement, was already in the possession of John Hancock, provided such Confidential Information was not obtained directly or indirectly from Abbott, its Affiliates or Licensees under an ongoing obligation of confidentiality; or (iv) is disclosed in a press release agreed to by both parties under Section 10.3 below.

10.3 Publicity Review. Without the prior written consent of the other party, neither party shall make any statement to the public regarding the execution and/or any other aspect of the subject matter of this Agreement and John Hancock shall not make any statement to the public regarding any work under the Research Program. Abbott may make statements to the public regarding work done under the Research Program (without reference to or mention of John Hancock) in accordance with its standard business practices. John Hancock and Abbott shall not disclose any terms or conditions of this Agreement to any third party without the prior consent of the other party, except as set forth above in this Section 10.3 or as required by applicable law, regulation or court order. The parties agree not to issue a press release announcing the execution of this Agreement.

**CONFIDENTIAL**  
**JH 005253**



-20-

ARTICLE 11  
TERM AND TERMINATION

11.1 Expiration. This Agreement shall expire upon satisfaction of Abbott's obligations to pay royalties and all other amounts under this Agreement.

11.2 Termination; Material Breach. It is the parties' express intent that consideration shall be given to remedying any breach of this Agreement through the payment of monetary damages or such other legal or equitable remedies as shall be appropriate under the circumstances and that there shall only be a limited right to terminate this Agreement under the following circumstances.

- (a) In the event that the Neutral, in accordance with the procedures set forth in Section 16.7, has issued a ruling that John Hancock has breached its obligation under Section 3.1 of this Agreement (obligation to make payments), and such ruling specified the actions to be taken by John Hancock on account of such breach, and John Hancock has failed to comply with the terms of such ruling within the time period specified therein for compliance, then, in addition to all other rights available to Abbott under law and equity, including its right to enforce such ruling in court, Abbott shall have the right to request that the Neutral terminate the Agreement as a result of John Hancock's failure to abide by the terms of this Agreement and such ruling.
- (b) In the event that the Neutral, in accordance with the procedures set forth in Section 16.7, has issued a ruling that Abbott has breached a material obligation under this Agreement, and such ruling specified the actions to be taken by Abbott on account of such breach, and Abbott has failed to comply with the terms of such ruling within the time period specified therein for compliance, then, in addition to all other rights available to John Hancock under law and equity, including its right to enforce such ruling in court, John Hancock shall have the right to request that the Neutral (i) terminate the Agreement and/or (ii) further rule that Abbott refund to John Hancock all Program Payments made by John Hancock hereunder (plus interest from the date such payments were originally made by John Hancock at the rate set forth in Section 9.4), each as a result of Abbott's failure to abide by the terms of this Agreement and such ruling.
- (c) In no event will either party be entitled to request that the Neutral terminate this Agreement as ~~described in this Section 11.1~~ or request a refund of Program Payments as described in this Section 11.2, if such party is then in breach of any Adverse Ruling of the Neutral; it being further understood in all cases that such request is not binding on the Neutral, but instead the Neutral shall rule on the request as he or she deems appropriate in light of all of the circumstances.

CONFIDENTIAL  
JH 005254

-21-

11.3 Effect of Expiration or Termination. Expiration or, if applicable, termination of this Agreement shall not relieve the parties of any obligation accruing prior to such expiration or termination. The provisions of Articles 8 (Royalty Reports and Accounting), 10 (Confidentiality), 11 (Term and Termination), 12 (Warranties and Indemnification) and 16 (Miscellaneous) shall survive the expiration or termination of this Agreement.

## ARTICLE 12 WARRANTIES AND INDEMNITY

12.1 John Hancock Representations and Warranties. John Hancock represents and warrants to Abbott that as of the Execution Date:

- (a) The execution and delivery of this Agreement and the performance of the transactions contemplated hereby have been duly authorized by all appropriate John Hancock corporate action. This Agreement constitutes John Hancock's valid and binding legal obligation, enforceable against it in accordance with its terms.
- (b) The performance by John Hancock of any of the terms and conditions of this Agreement on its part to be performed does not and will not constitute a breach or violation of its organizational documents or any other material agreement or understanding, written or oral, to which it is a party or any law, statute, rule or regulation by which it is bound.
- (c) No consent, approval, license or authorization of, or designation, declaration or filing with, any court or governmental authority is or will be required on the part of John Hancock in connection with the execution, delivery and performance by John Hancock of this Agreement or any other agreements or instruments executed and delivered by John Hancock in connection herewith or therewith, including, without limitation, any filings pursuant to federal or state securities laws or pursuant to any federal anti-trust laws.
- (d) Neither John Hancock nor any person acting on its behalf (i) has taken or will take any action which would subject this Agreement and the consummation of the transactions contemplated hereby to the registration or qualification requirements of any federal or state securities laws, (ii) has dealt with any broker, finder or other similar person in connection with the transactions contemplated by this Agreement or (iii) is under any obligation to pay any broker's fee, finder's fee or commission in connection with such transactions.

12.2 Abbott Representations and Warranties. Abbott represents and warrants to John Hancock that as of the Execution Date:

**CONFIDENTIAL**  
**JH 005255**



-22-

- (a) The execution and delivery of this Agreement and the performance of the transactions contemplated hereby have been duly authorized by all appropriate Abbott corporate action. This Agreement constitutes Abbott's valid and binding legal obligation, enforceable against it in accordance with its terms.
- (b) The performance by Abbott of any of the terms and conditions of this Agreement on its part to be performed does not and will not constitute a breach or violation of its organizational documents or any other agreement or understanding, written or oral, to which it is a party or any law, statute, rule or regulation by which it is bound.
- (c) No consent, approval, license or authorization of, or designation, declaration or filing with, any court or governmental authority is or will be required on the part of Abbott in connection with the execution, delivery and performance by Abbott of this Agreement or any other agreements or instruments executed and delivered by Abbott in connection herewith or therewith, including, without limitation, any filings pursuant to federal or state securities laws or pursuant to any federal anti-trust laws, except those consents, approvals, licenses, authorizations, and other requirements imposed by governmental authorities (both U.S. and foreign) and such declarations and filings with governmental authorities (both U.S. and foreign) required in the normal course of pharmaceutical research, development, marketing and sale.
- (d) Set forth on Exhibit 12.2(d) is the full name, chemical name, detailed description of the stage of development and current status, for each Program Compound. Also set forth on Exhibit 12.2(d) is a description of projected milestones and dates thereof, projected year of NDA filing, and projected costs to be incurred by Abbott during the Program Term, for each Program Compound. *[please complete Exhibit 12.2(d) (e.g., detailed description of stage of development and current status; projected milestones, year of NDA filing and costs)]* Such projections were prepared in good faith and with due care based on reasonable assumptions, and represent the reasonable estimate of Abbott based on information available as of the date of such projections and as of the date hereof; it being agreed that such projections do not constitute any warranty as to the future performance of the Program Compounds and that actual results may vary from such projections.
- (e) Set forth on Exhibit 12.2(e) is a list and description of all domestic and foreign patents, patent rights, patent applications and all patent applications that are in the process of being prepared that are owned by or registered in the name of Abbott, or of which Abbott is a licensee or in which Abbott has any right, which claim any of the Program Compounds (the "Patents"). Abbott solely owns all of the Patents, except as indicated on Exhibit 12.2(e). All of the material Patents have been duly filed in or

CONFIDENTIAL  
JH 005256

-23-

issued by the United States Patent and Trademark Office or the equivalent foreign patent office, as the case may be, and have been properly maintained and renewed in accordance with all applicable laws and regulations. With respect to the Patents that it does not own, Abbott has an exclusive and valid license thereunder to develop, make, have made, use, market and sell (with the right to sublicense) the applicable Program Compounds in the entire Territory (except with respect to (i) Italy, Abbott has such rights that are co-exclusive with Eisai Co. Ltd. for the Program Compound known as ABT-751 and (ii) Japan, Abbott has such rights that are co-exclusive with Taisho Pharmaceutical Co., Ltd. for the Program Compound known as ABT-773). To Abbott's knowledge, upon due inquiry and investigation consistent with using Commercially Reasonable Efforts, it is not necessary to obtain or license any patents, patent rights, inventions, copyrights, manufacturing processes, formulae, trade secrets, proprietary rights or know-how that it does not currently have in order to (i) develop, make, have made, use, market and sell the Program Compounds (except with respect to the Preclinical Programs) or (ii) conduct the Research Program as heretofore conducted and as proposed to be conducted (except with respect to the Preclinical Programs). Except as set forth in the In-License Agreements, the Program Compounds are owned exclusively by Abbott, free and clear of any liens or encumbrances of any other person and, to Abbott's knowledge, Abbott does not require the consent of any other person to develop, make, have made, use, market and sell the Program Compounds.

- (f) Except as set forth in Exhibit 12.2(f), Abbott has not received any communications alleging that, and no claim is pending or, to the knowledge of Abbott, threatened to the effect that, the operations of Abbott with respect to the Research Program or the Program Compounds infringe upon or conflict with (or will infringe or conflict with) the asserted rights of any other person under any domestic or foreign patent, trademark, service mark, copyright, trade secret, proprietary right or any other intellectual property right, and, except for the Preclinical Programs, there is no material basis known to Abbott for any such claim (whether or not pending or threatened). No claim is pending or, to the knowledge of Abbott, threatened to the effect that any of the Patents are invalid or unenforceable by Abbott, and there is no material basis known to Abbott for any such claim (whether or not pending or threatened). The publication of any material technical information with respect to the Program Compounds developed by and belonging to Abbott is subject to review and approval under Abbott's existing procedures.
- (g) Except as set forth in the In-License Agreements and customary employment and consulting agreements with Abbott's employees and consultants, there are no outstanding options, licenses, or agreements of any kind relating to the Patents or any of the Program Compounds or the transactions contemplated by this Agreement, which license the Patents or

-24-

any technical information developed in the course of the clinical development program to any third party to register, market or sell any of the Program Compounds or Products.

- (h) To the knowledge of Abbott with respect to the Research Program and each of the Program Compounds, Abbott is not now, and in performing its obligations hereunder will not be, in any way making an unlawful or wrongful use of any confidential information, know-how, or trade secrets of any other person.
- (i) Neither this Agreement, nor any Exhibit to this Agreement (including the compound reports attached as Exhibit 12.2(i) hereto (the "Compound Reports")) ~~contain~~ contains any untrue statement of material fact or omits to state any material fact necessary to make the statements contained herein or therein not misleading. There is no fact known to Abbott (other than generally available information concerning the pharmaceutical industry as a whole) as of the date of this Agreement that has not been disclosed in this Agreement or any Exhibit to this Agreement which has resulted in, or could reasonably be expected to result in, a material adverse effect on the prospects or condition (including safety, efficacy, scientific viability or commercial) of the Research Program or any of the Program Compounds.
- (j) Neither Abbott nor any person acting on its behalf (i) has taken or will take any action which would subject this Agreement and the consummation of the transactions contemplated hereby to the registration or qualification requirements of any federal or state securities laws, (ii) has dealt with any broker, finder or other similar person in connection with the transactions contemplated by this Agreement or (iii) is under any obligation to pay any broker's fee, finder's fee or commission in connection with such transactions.
- (k) There Other than generally publicized actions, proceedings or investigations concerning the pharmaceutical industry as a whole, there is no action, proceeding or investigation pending or, to the knowledge of Abbott, threatened which (i) questions the validity of this Agreement or any action taken or to be taken by Abbott pursuant thereto or (ii) which has resulted in, or could reasonably be expected to result in, a material adverse effect on the prospects or condition (including safety, efficacy, scientific viability or commercial) of the Research Program or any of the Program Compounds.
- (l) With respect to the Research Program and each of the Program Compounds, Abbott has (and in the future will have) obtained, to the extent permitted by law, from each of its employees, consultants, Affiliates and Subcontractors an agreement that reasonably protects Abbott's interest in the Program Inventions, Program Compounds and Products.

-25-

- (m) With respect to each Program Compound, since the date of its respective Compound Report, to the knowledge of Abbott, no condition, circumstance or fact has arisen (other than generally available information concerning the pharmaceutical industry as a whole) nor has Abbott made any change in the conduct of the Research Program which, individually or in the aggregate, has resulted in, or could reasonably be expected to result in, a material adverse effect on the prospects or condition (including safety, efficacy, scientific viability or commercial) of such Program Compounds.
- (n) Each In-License Agreement is valid, binding and in full force and effect, and there is no event which has occurred or exists, which constitutes or which, with notice and/or the passage of time, would constitute a material default or breach under any such contract by Abbott or, to Abbott's knowledge, any other party thereto, or would cause the acceleration of any obligation of any party thereto or give rise to any right of termination or cancellation thereof. Abbott has no reason to believe that the parties to each In-License Agreement will not fulfill their obligations thereunder in all material respects or that such parties do not have the right to grant the licenses granted thereunder. Abbott has no reason to believe that it will not fulfill its obligations under the In-License Agreements. Neither Under the Eisai Agreement, neither Abbott nor its Affiliates has the right to market, distribute or sell Products containing the Program Compound known as (i) ABT-751 in the Eisai Territory. ~~or (ii) ABT-773 in the Taishe Territory~~

12.3 No Conflict. Abbott and John Hancock represent and warrant that this Agreement does not, and will not, conflict with any other right or obligation provided under any other agreement or obligation that Abbott or John Hancock has with or to any third party.

12.4 Compliance with Law. Each party represents and warrants to the other that it will comply with all applicable laws, regulations and guidelines in connection with its performance of its obligations and rights pursuant to this Agreement, including the regulations of the United States and any other relevant nation concerning any export or other transfer of technology, services or products.

12.5 No Other Warranties. EACH PARTY TO THIS AGREEMENT AGREES THAT, EXCEPT FOR THE REPRESENTATIONS AND WARRANTIES CONTAINED IN THIS AGREEMENT, NEITHER PARTY MAKES ANY OTHER REPRESENTATIONS OR WARRANTIES, AND EACH HEREBY DISCLAIMS ANY OTHER REPRESENTATIONS OR WARRANTIES MADE BY ITSELF OR ANY OF ITS OFFICERS, DIRECTORS, EMPLOYEES, AGENTS, FINANCIAL AND LEGAL ADVISORS OR OTHER REPRESENTATIVES, WITH RESPECT TO THE EXECUTION AND DELIVERY OF THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED BY THIS AGREEMENT, NOTWITHSTANDING THE DELIVERY OR DISCLOSURE TO THE OTHER OR THE OTHER'S REPRESENTATIVES OF ANY DOCUMENTATION OR OTHER INFORMATION WITH RESPECT TO ANY ONE OR MORE OF THE FOREGOING.

-26-

12.6 General Indemnification of John Hancock. ~~Indemnification of John Hancock.~~

(a) Abbott shall indemnify and hold John Hancock and its Affiliates, agents, directors and employees harmless, and hereby forever releases and discharges John Hancock and its Affiliates, agents, directors and employees, from and against all Losses related to or arising out of, directly or indirectly, (i) any negligence, recklessness or intentional misconduct of Abbott or its Affiliates, agents, directors, employees, Subcontractors, licensees (including Licensees) or sublicensees in connection with the Research Program, Program Compounds or Products, or (ii) any manufacture, use, storage, distribution or sale of the Program Compounds or Products by anyone, including without limitation all Losses related to any personal injury or death, or (iii) any breach by Abbott of its representations, warranties or obligations hereunder, or (iv) the consummation of the transactions contemplated hereby, except, in each case, to the extent any such Losses are the result of (A) any breach by John Hancock of its representations, warranties or obligations hereunder, or (B) any negligence, recklessness, or intentional misconduct by John Hancock or its Affiliates, agents, directors, employees.

(b)

12.7 Indemnification Relating to Certain In-Licensed Compounds. Abbott shall indemnify and hold John Hancock and its Affiliates, agents, directors and employees harmless, and hereby forever releases and discharges John Hancock and its Affiliates, agents, directors and employees, from and against all Losses to the extent related to or arising out of, directly or indirectly, the fact that ~~(i) Abbott does not own Abbott's rights in~~ the Program Compounds known as ABT-773, ABT-492 and ABT-751 and ~~does not own~~ the Patents and other patent rights, copyrights, trade secret rights and other intellectual property rights related thereto ~~or (ii) such compounds and all of Abbott's rights with respect thereto are subject to arise from the Taisho Agreement, the Wakunaga Agreement and the Eisai Agreement, respectively, rather than being owned by Abbott as with the other Program Compounds.~~ Accordingly, by way of example and without limiting the foregoing, Abbott's indemnification obligation under this Section ~~12.6(b)~~ 12.7 will arise upon ~~(A)(i)~~ any impairment of Abbott's right to develop, make, use or sell such Program Compounds (and Products resulting therefrom) in the entire Territory because it does not own such Program Compounds or related intellectual property ~~or (B), as it does the other Program Compounds or (ii)~~ a breach by Abbott or any other person of any of the In-License Agreements; except, in each case, to the extent any such Losses are the result of (A) any breach by John Hancock of its representations, warranties or obligations hereunder, or (B) any negligence, recklessness, or intentional misconduct by John Hancock or its Affiliates, agents, directors, employees.

12.7

12.8 Procedure. If John Hancock or any of its Affiliates, agents, directors or employees (each, an "Indemnitee") intends to claim indemnification under this Article 12, it shall promptly notify Abbott (the "Indemnitor") of any Loss or action in respect of which the Indemnitee intends to claim such indemnification, and the Indemnitor shall have the right to participate in, and, to the extent the Indemnitor so desires, to assume the defense thereof with counsel selected by the Indemnitor; provided, however, that an Indemnitee shall have the right to retain its own counsel, with the fees and expenses of such counsel to be paid by the Indemnitor, if representation of such Indemnitee by the counsel retained by the Indemnitor would be



-27-

inappropriate due to actual or potential differing interests between such Indemnitee and any other party represented by such counsel in such proceedings. The indemnity obligation in this Article 12 shall not apply to amounts paid in settlement of any loss, claim, damage, liability or action if such settlement is effected without the consent of the Indemnitor, which consent shall not be withheld unreasonably or delayed. The failure to deliver notice to the Indemnitor within a reasonable time after the commencement of any such action, if materially prejudicial to its ability to defend such action, shall relieve the Indemnitor of any liability to the Indemnitee under this Article 12 only to the extent arising from the tardiness or absence of such notice, but the omission so to deliver notice to the Indemnitor will not relieve it of any liability that it may have to any Indemnitee otherwise than under this Article 12. The Indemnitee shall cooperate fully with the Indemnitor and its legal representatives in the investigation of any action, claim or liability covered by indemnification under this Article 12, at the expense of the Indemnitor.

~~12.8~~

12.9 Insurance. Abbott shall at its expense maintain, through self-insurance or otherwise, product liability insurance with respect to the development, manufacture, sale and use of Products and Program Compounds in such amounts and on such terms as Abbott customarily maintains with respect to its other similar products. Abbott shall maintain such insurance for so long as it continues to develop, manufacture or sell any Products or Program Compounds, and thereafter for so long as Abbott customarily currently maintains such insurance.

~~12.9~~

12.10 Acknowledgment. Abbott and John Hancock acknowledge that Abbott has not delivered or disclosed the contents of any of the In-License Agreements to John Hancock.

### ARTICLE 13 FORCE MAJEURE

Neither party shall be held liable or responsible to the other party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party including but not limited to fire, floods, embargoes, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, acts of God or acts, omission or delays in acting by any governmental authority; provided that such party shall provide the other party with prompt notice of the circumstances surrounding such a material failure or delay, after which the parties will amend this Agreement upon terms and conditions that are mutually agreeable to equitably account to the party that does not so fail or delay.

### ARTICLE 14 ASSIGNMENT

Except as expressly provided hereunder, this Agreement may not be assigned or otherwise transferred, nor may any right or obligations hereunder be assigned or transferred by either party without the consent of the other party; and, in addition, both parties acknowledge and

**CONFIDENTIAL**  
JH 005261

-28-

agree that the obligations of Abbott hereunder are personal to Abbott and that Abbott is uniquely qualified to perform them; provided, however, that either party shall be obligated to assign this Agreement and its rights and obligations hereunder in connection with the transfer or sale of all or substantially all of its business, or in the event of its merger or consolidation or change in control or similar transaction and in such event such party shall cause its successor or transferee in such transaction to assume all of the obligations of such party. Any permitted assignee shall assume all obligations of its assignor under this Agreement. Notwithstanding the foregoing, John Hancock shall have right to assign its right to payments without Abbott's consent, in whole or in part, hereunder (but not its obligations) to any other person and such other person shall be permitted to enjoy and exercise all of the rights of John Hancock assigned to it; provided that (i) if such assignee is located outside the United States, John Hancock shall notify Abbott at least sixty (60) days in advance, (ii) such assignee shall not be a direct competitor of Abbott (but no bank, insurance company or other institutional investor shall be deemed to be such a competitor) and (iii) there shall be no greater than five (5) such assignees at any one time. [open] Abbott agrees to cooperate with John Hancock and provide any further assurances and cooperation as reasonably requested by John Hancock with respect to such assignment(s) by John Hancock.

ARTICLE 15  
SEVERABILITY

Each party hereby agrees that it does not intend its execution and delivery hereof or its performance hereunder to violate any public policy, statutory or common laws, rules, regulations, treaty or decision of any government agency or executive body thereof of any country or community or association of countries. If and to the extent any term or provision of this Agreement is held to be invalid, illegal or unenforceable by a court or other governmental authority of competent jurisdiction, such invalidity, illegality or unenforceability shall not affect any other term or provision of this Agreement, which shall remain in full force and effect. The holding of a term or provision to be invalid, illegal or unenforceable in a jurisdiction shall not have any effect on the application of the term or provision in any other jurisdiction.

ARTICLE 16  
MISCELLANEOUS

16.1 Notices. Any consent, notice or report required or permitted to be given or made under this Agreement by one of the parties hereto to the other shall be in writing, delivered personally or by facsimile (and promptly confirmed by personal delivery, U.S. first class mail or courier), U.S. first class mail or courier, postage prepared (where applicable), addressed to such other party at its address indicated below, or to such other address as the addressee shall have last furnished in writing to the addressor and (except as otherwise provided in this Agreement) shall be effective upon receipt by the addressee.

CONFIDENTIAL  
JH 005262



-29-

If to John Hancock: John Hancock Life Insurance Company  
200 Clarendon Street, T-57  
Boston, MA 02117  
Attention: Bond & Corporate Finance Group  
Telephone: 617-572-9624  
Fax: 617-572-1628

copy to: John Hancock Life Insurance Company  
200 Clarendon Street, T-50  
Boston, MA 02117  
Attention: Investment Law Division  
Telephone: 617-572-9205  
Fax: 617-572-9268

and, if it relates to making or not making a royalty payment or Milestone Payment hereunder.

copy to: John Hancock Life Insurance Company  
200 Clarendon Street  
Boston, MA 02117  
Attention: Manager, Investment Accounting Division, B-3  
Fax: 617-572-9268 0628

If to Abbott: Abbott Laboratories  
Dept. 309, Bldg. AP30  
200 Abbott Park Road  
Abbott Park, IL 60064-3537  
Attention: President, Pharmaceutical Products Division  
Telephone: 847-938-6863  
Fax: 847-938-5383

copy to: General Counsel  
Abbott Laboratories  
Dept. 364, Bldg. AP6D  
100 Abbott Park Road  
Abbott Park, IL 60064-6020  
Telephone: 847-937-8905  
Fax: 847-938-6277

16.2 Applicable Law. The Agreement shall be governed by and construed in accordance with the internal laws of the State of Illinois. With respect to any action to enforce an Adverse Ruling as set forth in Section 16.7 below, Abbott, to the extent that it may lawfully do so, hereby consents to service of process, and to be sued, in the Commonwealth of Massachusetts and consents to the exclusive jurisdiction of the courts of the Commonwealth of Massachusetts and the United States District Court for the District of Massachusetts, as well as to the jurisdiction of all courts to which an appeal may be taken from such courts, for the purpose of any suit, action or other proceeding arising out of any of its obligations hereunder or thereunder

**CONFIDENTIAL**  
**JH 005263**

-30-

or with respect to the transactions contemplated hereby or thereby, and expressly waives any and all objections it may have as to venue in any such courts. Abbott further agrees that a summons and complaint commencing an action or proceeding in any of such courts shall be properly served and shall confer personal jurisdiction if served personally or by certified mail to it at its address for notices as provided in this Agreement or as otherwise provided under the laws of the Commonwealth of Massachusetts. THE PARTIES EACH IRREVOCABLY WAIVE ALL RIGHT TO A TRIAL BY JURY IN ANY SUIT, ACTION OR OTHER PROCEEDING INSTITUTED BY OR AGAINST IT IN RESPECT OF ITS OBLIGATIONS HEREUNDER OR THEREUNDER OR THE TRANSACTIONS CONTEMPLATED HEREBY OR THEREBY.

16.3 Entire Agreement. This Agreement contains the entire understanding of the parties with respect to the subject matter hereof. All express or implied agreements and understandings, either oral or written, with respect to the subject matter hereof heretofore made are expressly merged in and made a part of this Agreement. This Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by both parties hereto.

16.4 Headings. The captions to the several Articles and Sections hereof are not a part of this Agreement, but are merely guides or labels to assist in locating and reading the several Articles and Sections hereof.

16.5 Independent Contractors. It is expressly agreed that John Hancock and Abbott shall be independent contractors and that the relationship between the two parties shall not constitute a partnership, joint venture or agency. Neither John Hancock nor Abbott shall have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on the other, without the prior written consent of the other party to do so.

16.6 Performance By Affiliates, Licensees and Subcontractors. The parties recognize that Abbott may carry out certain obligations under this Agreement through performance by its Affiliates, Licensees and Subcontractors (but in no event shall that relieve Abbott of any of its obligations hereunder). Abbott guarantees that the activities of its Affiliates, Licensees and Subcontractors under this Agreement shall comply with this Agreement.

16.7 Alternative Dispute Resolution. The parties shall attempt to amicably resolve disputes arising between them regarding the validity, construction, enforceability or performance of the terms of this Agreement, and any differences or disputes in the interpretation of the rights, obligations, liabilities and/or remedies hereunder, which have been identified in a written notice from one party to the other, by good faith settlement discussions between the President of Abbott's Pharmaceutical Products Division and the Managing Director of John Hancock or his designee. The parties agree that any dispute that arises in connection with this Agreement, which cannot be amicably resolved by such representatives within thirty (30) days after the receipt of such written notice, shall be resolved by binding alternative dispute resolution in the manner described in Exhibit 16.7 attached hereto.

16.8 Waiver. The waiver by either party hereto of any right hereunder or the failure to perform or of a breach by the other party shall not be deemed a waiver of any other right

CONFIDENTIAL  
JH 005264

-31-

hereunder or of any other breach or failure by said other party whether of a similar nature or otherwise.

16.9 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

[the remainder of this page is intentionally blank]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first set forth above.

JOHN HANCOCK LIFE  
INSURANCE COMPANY

ABBOTT LABORATORIES

By: \_\_\_\_\_

By: \_\_\_\_\_

Name: \_\_\_\_\_

Name: \_\_\_\_\_

Title: \_\_\_\_\_

Title: \_\_\_\_\_

**CONFIDENTIAL**  
**JH 005265**

-32-

EXHIBIT 1.\_\_\_\_

ANNUAL RESEARCH PLAN - FIRST PROGRAM YEAR

EXHIBIT 1.\_\_\_\_

EISAI TERRITORY

1. Bhutan
2. Brunei
3. Cambodia
4. People's Republic of China
5. Republic of China (Taiwan)
6. India
7. Indonesia
8. Japan
9. Democratic People's Republic of Korea (North Korea)
10. Republic of Korea
11. Laos
12. Macao
13. Malaysia
14. Mongolia
15. Myanmar
16. Nepal
17. Pakistan
18. Papua New Guinea
19. Philippines
20. Singapore
21. Sri Lanka
22. Thailand
23. Vietnam

CONFIDENTIAL  
JH 005266

-33-

EXHIBIT 1.\_\_\_\_

PROGRAM COMPOUNDS

Program compounds:

	ABT-627 (Endothelin antagonist) - phase III
[Taisho]	ABT-773 (Ketolide antibiotic) - phase III
	ABT-594 (Cholinergic channel modulator) - late phase II
[Wakunaga]	ABT-492 (Quinolone antibiotic) - phase I
	ABT-510 (Thrombospondin peptide) - phase I
	ABT-518 (Matrix metalloproteinase inhibitor) - phase I
[Eisai]	ABT-751 (Antimitotic) - phase I

Preclinical programs:

Farnesyl transferase inhibitor (FTI) - late preclinical program  
Dopamine Receptor Agonist for Erectile Dysfunction (ED) - late preclinical program

EXHIBIT 1.[38]

EXAMPLE OF PROGRAM RELATED COSTS FOR ONE PROGRAM COMPOUND

EXHIBIT 6.3

CURRENT STAGE OF CLINICAL DEVELOPMENT FOR EACH PROGRAM COMPOUND

EXHIBIT 16.7

ALTERNATIVE DISPUTE RESOLUTION

*[subject to review by CHS litigation department]*

The parties recognize that a bona fide dispute as to certain matters may arise from time to time during the term of this Agreement which relates to either party's rights and/or obligations. To have such a dispute resolved by this Alternative Dispute Resolution ("ADR") provision, a party first must send written notice of the dispute to the other party for attempted resolution by good faith negotiations between the Managing Director of John Hancock and the Senior Vice President, Pharmaceutical Products Division, of Abbott (or their equivalents) of the affected subsidiaries, divisions, or business units within forty-five (45) days after such notice is received (all references to "days" in this ADR provision is to calendar days, unless the final day of a period of days hereunder falls on a Saturday, Sunday or federal holiday, in which case the end of such period shall be the first day following that is not a Saturday, Sunday or federal holiday).

Any negotiations regarding a dispute shall be treated as settlement negotiations for purposes of the Federal Rules of Evidence and any similar state rules of evidence. Such negotiations shall not be admissible in any subsequent ADR hearing.

CONFIDENTIAL  
JH 005267

-34-

If the matter has not been resolved within forty-five (45) days of the notice of dispute, or if the parties fail to meet within such forty-five (45) days, either party may initiate an ADR proceeding as provided herein. The parties shall have the right to be represented by counsel in such a proceeding.

1. To begin an ADR proceeding, a party shall provide written notice to the other party of the issues to be resolved by ADR. Within twenty-eight (28) days after its receipt of such notice, the other party may, by written notice to the party initiating the ADR, add additional issues to be resolved within the same ADR.

2. Within forty-five (45) days following receipt of the original ADR notice, the parties shall select a mutually acceptable neutral individual (the "Neutral") to preside in the resolution of any disputes in this ADR proceeding. If the parties are unable to agree on a mutually acceptable Neutral within such period, the parties shall request that the American Arbitration Association of \_\_\_\_\_, New York ("AAA") in accordance with its Commercial Arbitration Rules (the "Rules") select the Neutral pursuant to the following procedures:

(a) The AAA shall submit to the parties a list of not less than five (5) candidates within fourteen (14) days after receipt of the request from the parties, along with a Curriculum Vitae for each candidate. No candidate shall be an employee, director, or shareholder of either party or any of their subsidiaries or affiliates.

(b) Such list shall include a statement of disclosure by each candidate of any circumstances likely to affect his or her impartiality.

(c) Each party shall number the candidates in order of preference (with the number one (1) signifying the greatest preference) and shall deliver the list to the AAA within seven (7) days following receipt of the list of candidates. If a party believes a conflict of interest exists regarding any of the candidates, that party shall provide a written explanation of the conflict to the AAA along with its list showing its order of preference for the candidates. Any party failing to return a list of preferences on time shall be deemed to have no order of preference.

(d) If the parties collectively have identified fewer than three (3) candidates deemed to have conflicts, the AAA immediately shall designate as the Neutral the candidate for whom the parties collectively have indicated the greatest preference. If a tie should result between two candidates, the AAA may designate either candidate. If the parties collectively have identified three (3) or more candidates deemed to have conflicts, the AAA shall review the explanations regarding conflicts and, in its sole discretion, may either (i) immediately designate as the Neutral the candidate for whom the parties collectively have indicated the greatest preference, or (ii) issue a new list of not less than five (5) candidates, in which case the procedures set forth in subparagraphs 2(a) - 2(d) shall be repeated.

3. No earlier than twenty-eight (28) days or later than one-hundred eighty (180) days after selection, the Neutral shall hold a hearing to resolve each of the issues identified by the parties. The ADR proceeding shall take place in New York, NY, or at such other location agreed upon by the parties. The language of the ADR proceeding shall be English.

CONFIDENTIAL  
JH 005268

-35-

4. At least fourteen (14) days prior to the hearing, each party shall submit the following to the other party and the Neutral:

- (a) a copy of all exhibits on which such party intends to rely in any oral or written presentation to the Neutral;
- (b) a list of any witnesses such party intends to call at the hearing, and a short summary of the anticipated testimony of each witness;
- (c) a proposed ruling on each issue to be resolved, together with a request for a specific damage award or other remedy for each issue;
- (d) a brief in support of such party's proposed rulings and remedies, provided that the brief shall not exceed twenty (20) pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

Any and all discovery (including depositions, interrogatories, requests for admissions, and production of documents) shall be conducted in accordance with the Rules.

5. The hearing shall be governed by the following rules:

- (a) Each party shall be entitled, but not required, to make an opening statement, to present regular and rebuttal testimony, documents or other evidence, to cross-examine witnesses, and to make a closing argument. Cross-examination of witnesses shall occur immediately after their direct testimony.
- (b) The party initiating the ADR shall begin the hearing and, if it chooses to make an opening statement, shall address not only issues it raised but also any issues raised by the responding party. The responding party, if it chooses to make an opening statement, also shall address all issues raised in the ADR. Thereafter, the presentation of regular and rebuttal testimony and documents, other evidence, and closing arguments shall proceed in the same sequence.
- (c) Settlement negotiations shall not be admissible under any circumstances. As to all other matters, the Neutral shall have sole discretion regarding the admissibility of any evidence.

6. Within seven (7) days following completion of the hearing, each party may submit to the other party and the Neutral a post-hearing brief in support of its proposed rulings and remedies.

7. The Neutral shall issue a written ruling on each disputed issue within fourteen (14) days following completion of the hearing.

8. The Neutral shall be paid a reasonable fee plus expenses. These fees and expenses, along with the reasonable legal fees and expenses of the prevailing party (including all expert witness fees and expenses), the fees and expenses of a court reporter, and any expenses for a hearing room, shall be paid as follows:

- (a) If the Neutral rules in favor of one party on all disputed issues in the ADR, the losing



-36-

party shall pay 100% of such fees and expenses.

(b) If the Neutral rules in favor of one party on some issues and the other party on other issues, the Neutral shall issue with the rulings a written determination as to how such fees and expenses shall be allocated between the parties. The Neutral shall allocate fees and expenses in a way that bears a reasonable relationship to the outcome of the ADR, with the party prevailing on more issues, or on issues of greater value or gravity, recovering a relatively larger share of its legal fees and expenses.

9. The rulings of the Neutral and the allocation of fees and expenses shall be binding, and may be entered as a final judgment in any court having jurisdiction. The rulings of the Neutral shall only be reviewable to the extent permitted by the Rules or by the Uniform Arbitration Act.

10. Except as provided in paragraph 9 or as required by law, the existence of the dispute, any settlement negotiations, the ADR hearing, any submissions (including exhibits, testimony, proposed rulings, and briefs), and the rulings shall be deemed Confidential Information. The Neutral shall have the authority to impose sanctions for unauthorized disclosure of Confidential Information.

11. Notwithstanding anything herein to the contrary, the Neutral may, in his or her sole discretion, extend or broaden the time periods and page lengths set forth above consistent with providing, as a foremost objective, each party an opportunity to present fairly its claims and/or defenses while also providing, as an secondary objective, an efficient ADR.

----- COMPARISON OF HEADERS -----

-HEADER 1-

-ii-

C

-HEADER 2-

-i-

-HEADER 3-

Header Discontinued

----- COMPARISON OF FOOTERS -----

-FOOTER 1-

**CONFIDENTIAL**  
**JH 005270**

-37-

**CONFIDENTIAL**  
JH 005271

**PLs' LO**

Dec. 1. 2000 3:13PM CORPORATE LICENSING

NO. 8612 P. 1



## ABBOTT LABORATORIES

## Facsimile Transmittal

Corporate Licensing  
100 Abbott Park Road,  
Abbott Park, IL 60064

From: Philip M. Deemer *pl*

Dept. 435 Bldg. AP6D

PHONE NO: (847) 937-4444

FAX NO. (847) 938-5852

TO: Arthur Higgins

Date: December 1, 2000

FAX NO: 8-5383

RECEIVED

# OF PAGES: 1

(Including Cover Page)

DEC 1 2000

RE: Hancock

STEVE J. WEGER, JR.

On November 27, I informed John Hancock that you and other Abbott senior management needed additional time to evaluate the new proposed deal structure. I told them that the new deal structure was received less favorably than the original structure and that there also may be some accounting issues with the new structure (Loughery is OK with it). In addition, I told them that there were a few contract issues to straighten out (not-related to the new deal structure). I told them we would send these proposed revised changes by the end of this week or the beginning of next week and that I would update them as to the status of the senior management review shortly thereafter.

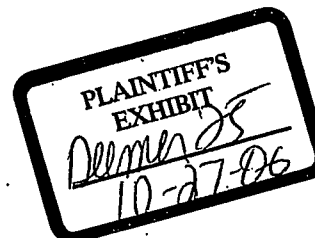
At least by December 8, I feel I need to tell them that our management is less enthusiastic about moving forward due to the new deal structure and to propose a meeting date with them during the week of December 11 to discuss possible options to enhance the effectiveness. I would anticipate receptivity to identifying possible improvement but I would not anticipate reverting back to the original structure unless there is a change in the portfolio or possibly an IOU.

The week of December 18, I assume that I will have pushed them as far as possible with alternative structure options and I will need to tell them that management wants to postpone a final decision until the new year. (I will of course inform you as to how well this is received.)

In January, assuming John Hancock is still interested in going forward, and assuming we decide to proceed, there may be a last opportunity for some modification of the portfolio.

In the event we decide not to proceed, there may be some opportunities with HPD or ADD portfolios to lessen the impact to John Hancock.

cc: Steve Weger  
8 5968



CONFIDENTIAL  
AL 001946

**PLs' LW**

NOV. 20. 2003 8:23AM

NO. 1275 P. 20

# ANALGESIA VENTURE

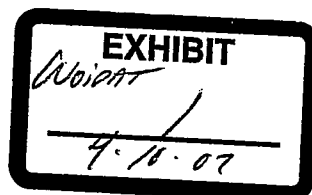
## 2001 PLAN

Revised 1/26/01

To:

John Leonard  
Chris Silber  
George Carter  
Bruce McCarthy  
Mike Blamesen  
Steve Cohen  
Mike Higgins  
Mike Comilla  
Matt Russell  
Tom Woldat  
Barbara Massa  
Marleen Verhinden

Highly Confidential



ABBT0503356

NOV. 20. 2003 8:23AM

NO. 1275 P. 21

**Analgesia Venture  
2001 PLAN Review (Pass II)  
Table of Contents**

1	Summary of Projects
2	ABT-594 Key Statistics
3	ABT-594 Grants
4-5	ABT-594 Project Expense
6	ABT-089 Key Statistics
7	ABT-089 Grants
8	ABT-089 Project Expense
9	NPS 1776 Key Statistics
10	NPS 1776 Grants
11	NPS 1776 Project Expense
12	ABS-103 Key Statistics
13	ABS-103 Grants
14	ABS-103 Project Expense
15	ABT-963 Key Statistics
16	ABT-963 Grants
17	ABT-963 Project Expense
18	Venture Functional Expense
19	Blue Plan Summary



NOV. 20. 2003 8:24AM

NO. 1275 P. 22

7

**Analgesia Venture  
Summary  
2001 PLAN Pass II**

	2001 Target	2000 AGU	2001 PLAN	Target vs PLAN Fav(Unfav) Var
ABT - 594	8,900	14,411	9,307	(407) a
ABT - 089	"	3,000	613	(613) b
NPS 1776	"	"	537	(537) c
ABS - 103	"	"	"	" b
ABT - 963	"	4,000	1,186	(1,186) b
Venture Total	<u>8,900</u>	<u>21,411</u>	<u>11,643</u>	<u>(2,743)</u>

a Includes a \$120,000 charge from SPD not in Oracle

b Completion of work started in 2000, bringing it to a logical holding position.

c Includes a \$490,000 charge from SPD included in Oracle in error.



2001 PLAN		2002 PLAN		2003 PLAN		2004 PLAN		2005 PLAN		2006 PLAN		2007 PLAN		2008 PLAN		2009 PLAN		2010 PLAN		2011 PLAN		2012 PLAN		2013 PLAN		2014 PLAN		2015 PLAN		2016 PLAN		2017 PLAN		2018 PLAN		2019 PLAN		2020 PLAN		2021 PLAN		2022 PLAN		2023 PLAN		2024 PLAN		2025 PLAN		2026 PLAN		2027 PLAN		2028 PLAN		2029 PLAN		2030 PLAN		2031 PLAN		2032 PLAN		2033 PLAN		2034 PLAN		2035 PLAN		2036 PLAN		2037 PLAN		2038 PLAN		2039 PLAN		2040 PLAN		2041 PLAN		2042 PLAN		2043 PLAN		2044 PLAN		2045 PLAN		2046 PLAN		2047 PLAN		2048 PLAN		2049 PLAN		2050 PLAN		2051 PLAN		2052 PLAN		2053 PLAN		2054 PLAN		2055 PLAN		2056 PLAN		2057 PLAN		2058 PLAN		2059 PLAN		2060 PLAN		2061 PLAN		2062 PLAN		2063 PLAN		2064 PLAN		2065 PLAN		2066 PLAN		2067 PLAN		2068 PLAN		2069 PLAN		2070 PLAN		2071 PLAN		2072 PLAN		2073 PLAN		2074 PLAN		2075 PLAN		2076 PLAN		2077 PLAN		2078 PLAN		2079 PLAN		2080 PLAN		2081 PLAN		2082 PLAN		2083 PLAN		2084 PLAN		2085 PLAN		2086 PLAN		2087 PLAN		2088 PLAN		2089 PLAN		2090 PLAN		2091 PLAN		2092 PLAN		2093 PLAN		2094 PLAN		2095 PLAN		2096 PLAN		2097 PLAN		2098 PLAN		2099 PLAN		2100 PLAN		2101 PLAN		2102 PLAN		2103 PLAN		2104 PLAN		2105 PLAN		2106 PLAN		2107 PLAN		2108 PLAN		2109 PLAN		2110 PLAN		2111 PLAN		2112 PLAN		2113 PLAN		2114 PLAN		2115 PLAN		2116 PLAN		2117 PLAN		2118 PLAN		2119 PLAN		2120 PLAN		2121 PLAN		2122 PLAN		2123 PLAN		2124 PLAN		2125 PLAN		2126 PLAN		2127 PLAN		2128 PLAN		2129 PLAN		2130 PLAN		2131 PLAN		2132 PLAN		2133 PLAN		2134 PLAN		2135 PLAN		2136 PLAN		2137 PLAN		2138 PLAN		2139 PLAN		2140 PLAN		2141 PLAN		2142 PLAN		2143 PLAN		2144 PLAN		2145 PLAN		2146 PLAN		2147 PLAN		2148 PLAN		2149 PLAN		2150 PLAN		2151 PLAN		2152 PLAN		2153 PLAN		2154 PLAN		2155 PLAN		2156 PLAN		2157 PLAN		2158 PLAN		2159 PLAN		2160 PLAN		2161 PLAN		2162 PLAN		2163 PLAN		2164 PLAN		2165 PLAN		2166 PLAN		2167 PLAN		2168 PLAN		2169 PLAN		2170 PLAN		2171 PLAN		2172 PLAN		2173 PLAN		2174 PLAN		2175 PLAN		2176 PLAN		2177 PLAN		2178 PLAN		2179 PLAN		2180 PLAN		2181 PLAN		2182 PLAN		2183 PLAN		2184 PLAN		2185 PLAN		2186 PLAN		2187 PLAN		2188 PLAN		2189 PLAN		2190 PLAN		2191 PLAN		2192 PLAN		2193 PLAN		2194 PLAN		2195 PLAN		2196 PLAN		2197 PLAN		2198 PLAN		2199 PLAN		2200 PLAN		2201 PLAN		2202 PLAN		2203 PLAN		2204 PLAN		2205 PLAN		2206 PLAN		2207 PLAN		2208 PLAN		2209 PLAN		2210 PLAN		2211 PLAN		2212 PLAN		2213 PLAN		2214 PLAN		2215 PLAN		2216 PLAN		2217 PLAN		2218 PLAN		2219 PLAN		2220 PLAN		2221 PLAN		2222 PLAN		2223 PLAN		2224 PLAN		2225 PLAN		2226 PLAN		2227 PLAN		2228 PLAN		2229 PLAN		2230 PLAN		2231 PLAN		2232 PLAN		2233 PLAN		2234 PLAN		2235 PLAN		2236 PLAN		2237 PLAN		2238 PLAN		2239 PLAN		2240 PLAN		2241 PLAN		2242 PLAN		2243 PLAN		2244 PLAN		2245 PLAN		2246 PLAN		2247 PLAN		2248 PLAN		2249 PLAN		2250 PLAN		2251 PLAN		2252 PLAN		2253 PLAN		2254 PLAN		2255 PLAN		2256 PLAN		2257 PLAN		2258 PLAN		2259 PLAN		2260 PLAN		2261 PLAN		2262 PLAN		2263 PLAN		2264 PLAN		2265 PLAN		2266 PLAN		2267 PLAN		2268 PLAN		2269 PLAN		2270 PLAN		2271 PLAN		2272 PLAN		2273 PLAN		2274 PLAN		2275 PLAN		2276 PLAN		2277 PLAN		2278 PLAN		2279 PLAN		2280 PLAN		2281 PLAN		2282 PLAN		2283 PLAN		2284 PLAN		2285 PLAN		2286 PLAN		2287 PLAN		2288 PLAN		2289 PLAN		2290 PLAN		2291 PLAN		2292 PLAN	
-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--	-----------	--

ABBT0503360

NOV. 20. 2003 8:24AM

NO. 1275 P. 25

**PHARMACEUTICAL PRODUCTS RESEARCH AND DEVELOPMENT**  
**2000 AUGUST UPDATE / 2001 PLAN**  
**G0-143010 CCM ABT594 (BASE & ORAL PAIN)**

4

	(\$000)				
	2000	2000	FAV/(UNFAV) AUG. UPD VS. APR. UPD.	2001 PLAN	FAV/(UNFAV) PLAN VS. AUG. UPD.
26-Jan-01					
4:04 PM					
<b>PPD INVESTIGATIONAL DR</b>					
PPD Investigational Drug QA	23	55	(32)	86	(32)
	23	55	(32)	86	(32)
<b>Venture Management</b>					
Analgesia/CCM Venture	4,739	4,493	246	3,988	505
	4,739	4,493	246	3,988	505
<b>Discovery</b>					
Advanced Technology	25	50	(25)	26	24
Neurological & Urological Res	---	---	---	51	(51)
	25	50	(25)	77	(28)
<b>Drug Safety</b>					
Experimental Science	23	70	(46)	187	(118)
Clinical Drug Analysis	290	290	---	409	(120)
Toxicology	1,366	896	471	233	663
Pathology	604	572	32	493	79
Comparative Medicine	591	591	---	34	557
Strategic & Exploratory Science	4	---	4	7	(7)
	2,877	2,417	460	1,362	1,055
<b>Pharm Analytical R&amp;D</b>					
ANALYTICS DEV & SUPPORT	791	879	(88)	641	238
FORMULATION DEV & SUPPORT	764	745	19	226	519
CLINICAL FINISHING	403	607	(204)	145	462
PROJECT MGMT SUPPORT	197	178	20	63	115
	2,155	2,409	(254)	1,075	1,334
<b>PHASE-I CENTER</b>					
Phase-I Admin/Pharmacokinetics	185	185	---	259	(74)
ACPRU	23	25	(2)	367	(343)
	208	210	(2)	627	(417)
<b>Development Operations</b>					
Data Management	475	475	---	259	216
Statistics	160	171	(11)	129	42
ABBOTT RES & LIBRARY INF-ARL	89	89	---	140	(51)
	724	735	(11)	528	207
<b>Regulatory Affairs</b>					
Regulatory Affairs	20	20	---	151	(131)
Research QA	131	80	50	82	(1)
	151	100	50	232	(132)
<b>Medical Affairs</b>					
Genetics/Admin	---	---	---	2	(2)
Medical Services	53	53	---	10	43
Outcomes Res./Admin.	42	42	---	37	5
	95	95	---	49	46
<b>Administration</b>					
R&D Operations/Project Services	75	43	32	45	(2)
	75	43	32	45	(2)
<b>AI MANPOWER</b>					
International Manpower	50	20	30	53	(33)
Friday, January 26, 2001 4:04:48 PM					
PROJECT GLOBAL PPD REPORT BY PROJ SUBDIV					

Page 1 of 4

Highly Confidential

ABBT0503361

NOV. 20. 2003 8:24AM

NO. 1275 P. 26

2000 AUGUST UPDATE / 2001 PLAN  
G0-143010 CCM ABT594 (BASE & ORAL PAIN)

	2000 APU	2000 AGU	FAV/(UNFAV) AUG. UPD VS. APR. UPD.	2001 PLAN	FAV/(UNFAV) PLAN VS. AUG. UPD.
26-Jan-01 4:04 PM	50	20	30	53	(33)
PPD R&D SERVICES PURCH	235	235	---	---	235
SPD Services Purchased	235	235	---	---	235
CLINICAL GRANTS	3,000	2,800	200	1,065	1,735
CLINICAL GRANTS	3,000	2,800	200	1,065	1,735
	14,357	13,661	696	9,287	4,474

SPD

120  
9,307

Friday, January 26, 2001 4:04:48 PM

PROJECT GLOBAL PPD REPORT BY PROJ SUBDIV

Page 2 of 4

Highly Confidential

ABBT0503362